PHARMA AND LIFESCIENCES INDUSTRY

– Certain Tax, Regulatory and Governance Aspects

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Pharma and Lifesciences Industry

— Certain Tax, Regulatory and Governance Aspects

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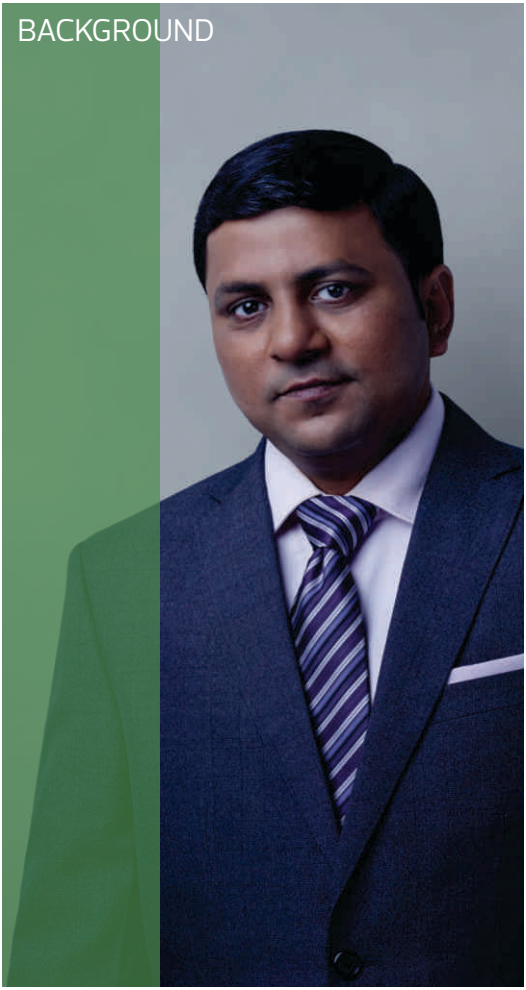
BACKGROUND



Chapter 1 Background

1.1 Pharmaceutical Industry in India

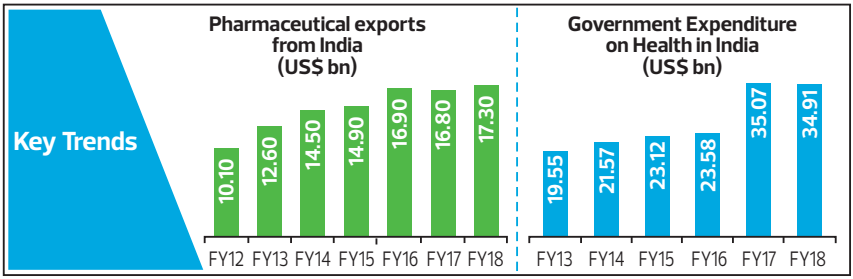
- The pharmaceutical industry in India ranks 3rd in the world in terms of volume and 14th in terms of value according to Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers. The country's pharmaceutical industry is expected to expand at a compound annual growth rate (CAGR) of 22.4% over 2015–20 to reach US$ 55 billion.

- Indian drugs are exported to more than 200 countries in the world, with the U.S. as the key market. Generic drugs account for 20 % of global exports in terms of volume, making the country the largest provider of generic medicines globally and expected to expand even further in coming years. India's pharmaceutical exports stood at US$ 17.27 billion in 2017–18. 31% of these exports from India were made to the U.S. Hyderabad, Mumbai, Bangalore, Vapi, Ankleshwar, Vadodara and Ahmedabad are the major pharmaceutical hubs of India. The drugs and pharmaceuticals sector attracted cumulative FDI inflows worth US$ 15.83 billion between April 2000 and June 2018, according to data released by the Department of Industrial Policy and Promotion (DIPP).

  (Source: https://www.ibef.org/industry/pharmaceutical-india.aspx)

- Indian pharmaceutical market grew 5.5 % in calendar year (CY) 2017 in terms of moving annual turnover. In March 2018, the market grew at 9.5 % year-on-year with sales of INR 10,029 crore (US$ 1.37 billion).

- The table below summarises certain key trends in terms of exports and Government expenditure on this industry.



Pharmaceutical companies operate in one of the most dynamic and heavily regulated environments. Changes in regulations in terms of stringent quality aspects by leading drug regulatory bodies such as U.S. Food and Drug Administration (USFDA), Therapeutic Goods Administration (TGA, Australia) and the European Medicines Agency (EMEA) have increased the significance of regulatory compliance management for drug manufacturers and suppliers. Pharma companies across the globe are obliged to alter their compliance practices to conform to changes in regulations and stringent CGMP compliances.

1.2 Food and Drug Administration in India

- The goals of FDA (which became operational in India in 2008) are to obtain information to help make better regulatory decisions about the products from India that are being developed and exported for the U.S. market. This includes medical products being reviewed for marketing authorization in the U.S. and the safety assessment of products that are already in the U.S. market. Hence U.S. FDA is relevant for those companies who export their products to the U.S. Market. FDA activities in India include:

    1. Conducting inspections of medical products and food facilities that are exported to U.S.
    2. Engaging with Indian regulatory authorities to build confidence in each other and develop quality standards.
    3. Partnering with Indian counterpart agencies on bilateral initiatives.
    4. Assisting and training Indian regulators, Indian pharmaceutical and foods industries and stakeholders on developing and maintaining the quality, safety and effectiveness of medical products and foods.
    5. Building and strengthening relationships with the government of India by supporting the mission of the U.S. Embassy.

- Recent experience in Indian pharma industries: Many Indian pharma manufacturers are facing stringent reviews and non-conformities with

norms of USFDA regulations and hence many import alerts and warning letters have been issued by USFDA Inspectors. During inspections of manufacturing facilities by USFDA inspectors, they have observed many deficiencies in quality management systems in terms of violations of Current Good Manufacturing Practices (CGMP) norms, data integrity and documentation issues, quality control or analytical related issues, stability study and transportation study related, equipment and utility qualifications related non compliances, improper failure investigations, etc.

- To mitigate above deficiencies, an efficient quality risk management,a good quality assurance system and superior governance systems are necessary.

1.3 Concept of US FDA

- The Food and Drug Administration (FDA or US FDA) is a federal agency of the United States' Department of Health and Human Services, one of the United States federal executive departments. The FDA is responsible for protecting and promoting public health through the control and supervision of food safety, tobacco products, dietary supplements, prescription and over-the-counter pharmaceutical drugs (medications), vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting devices (ERED), cosmetics, animal foods & feed and veterinary products by regulating the manufacturing, marketing, and distribution.

- US FDA oversees regulatory activities for those companies who export their pharmaceuticals and life science products to the U.S. Market in order to identify quality issues before they impact the production.

- The FDA has adopted a new risk-based paradigm for addressing its role as an oversight agency for the pharmaceutical industry. FDA guidelines state that the agency must inspect domestic drug manufacturing establishments at least once in every 2 years. Also the CGMP is necessary to be complied. Clearly, regulatory oversight is a critical component for

ensuring pharmaceutical quality and efficacy.

- During the development and production life cycle of human drugs, vaccines, and other biological products, FDA acts as the supervisory agency, assuring that industry best practices are followed.

- Furthermore, FDA wants oversight to ensure that industry approved steps are followed for identifying and isolating problems with such issues as contaminants and failed processes and assurance on compliance of CGMP guidelines. Additional areas of compliance ensure that appropriate Corrective and Preventive Actions (CAPA) are taken.

- FDA also plays a significant role in the nation's counterterrorism capability. FDA fulfills this responsibility by ensuring the security of the food supply and by fostering development of medical products to respond to deliberate and naturally emerging public health threats.

- The following is a list of traditionally-recognized product categories that fall under FDA's regulatory jurisdiction; however, this is not an exhaustive list:

Subjects	Includes
Foods	– Dietary supplements – Bottled water – Food additives – Infant formulas – Other food products
Drugs	– Prescription drugs (both brand-name and generic) – Non-prescription (over-the-counter) drugs
Biologics	– Vaccines – Blood and blood products – Cellular and gene therapy products – Tissue and tissue products – Allergenics

Subjects	Includes
Medical Devices	– Simple items like tongue depressors and bedpans – Complex technologies such as heart pacemakers
	– Dental devices – Surgical implants and prosthetics
Electronic Products that give off radiation	– Microwave ovens – X-ray equipment – Laser products – Ultrasonic therapy equipment – Mercury vapor lamps – Sunlamps
Cosmetics	– Color additives found in makeup and other personal care products – Skin moisturizers and cleansers – Nail polish and perfume
Veterinary Products	– Livestock feeds – Pet foods – Veterinary drugs and devices
Tobacco Products	– Cigarettes & Cigarette tobacco – Roll-your-own tobacco – Smokeless tobacco

1.4 Technical Aspects of Pharmaceuticals Industry

1.4.1 Drug Discovery and Development Solutions (DDDS)

DDDS business offers integrated services platform across target validation, discovery, pre-clinical and clinical development.

1.4.2 Radio-pharmaceuticals

The focus of radio-pharmaceuticals is on nuclear medicine, imaging and therapeutic agent. Applications of these products include cardiology, oncology, thyroid uptake and scans, lung scans, kidney and brain imaging and bone scans.

1.4.3 Various other businesses under pharma industry are as follows:

Generics	Allergenic Extracts	Major therapeutic and diagnostic extracts for allergy derived from pollens, animals and stinging insect's venoms.
	Dosage Form	Provider of high quality finished dosage forms (Tablets and Capsules).
CMO	Sterile & Non Sterile Products	CMO services for lyophilized products, liquid fills, biologics, suspensions, WFI/diluents, clinical trial quantities, ointment, cream, liquid, etc.
Healthcare		Providing affordable high-quality health care services in India as well as abroad.

1.4.4 Structure of Indian Pharmaceutical Industries

The Indian pharmaceutical industry comprises of API, Formulations, CRMS and Biosimilars.

Active Pharmaceutical Industries (APIs)	• API is the ingredient in the drug which is biologically active and is produced in the initial phase of the drug manufacturing. • API is referred to as input or raw materials in the manufacturing of formulation.
Formulations	• The final end products in the manufacturing of drugs which can directly be consumed by the patients. These are generally in the form of tablets, capsules and injectable. • The formulations sector in India is a highly fragmented market comprising a large number of manufacturers as well as a wide product range.
Contract Research and Manufacturing Services (CRAMS)	• This term refers to the arrangement of outsourcing of research services as well as the task of manufacturing products to those organizations providing these services at relatively reduced cost. • It involves the usage of comprehensive research and development coupled with the need for extensive manufacturing facilities.

Biosimilars	• These are generic or the follow-on versions of the original biological medicines and drugs. • The process of manufacturing of a biosimilar can be undertaken when the original product is being protected through patent exclusivity. "Biosimilars are a type of biological product that are licensed (approved) by the FDA because they are similar to an already approved biological product, known as biological reference product and have been shown to have no clinically meaningful difference from the reference product."

Chapter 2

COMPLIANCE CALENDER

Chapter 2 Compliance Calender

2.1 Background

This chapter deals with compliances under certain laws. In India, there are numerous laws which provide for compliances on a regular basis. Below is the list of significant compliances under Income-tax Act, FEMA, GST, Labour Laws, etc. It may be noted that this is not a comprehensive list which needs to be developed in each case based on the nature of operations.

Sr. No.	Particulars	Due Dates
2.1.1	**Fema Compliances**	
i.	Annual Performance report in Form APR	31st December every year
ii.	Annual return of foreign liabilities and assets (FLA) in form FLA	15thJuly every year
iii.	FC GPR / SMF	Within 30 days from date of issue of shares upon receipt of inward investment
iv.	ECB returns in Form ECB-2	Within 7 working days from the close of the month
v.	FDI in Advance Reporting Form	30 days of receipt of money
vi.	Non-resident person acquiring property in India in IPI Form.	90 days from the date of acquisition of immovable property
2.1.2	**Income Tax Compliances**	
A	**TDS/TCS Compliance**	
i.	Return cum challan in Form 26QB for 1% TDS on transfer of immovable property under section 194-IA	7 days from end of the month in which deduction is made.
ii.	TDS/TCS statements for other payments in Form 24Q/26Q/27Q/27EQ	31 days from the end of quarter for 1st, 2nd, 3rd & 4th quarter of the year.
iii.	TDS statements in Form 26QB	30 days from the end of the month in which deduction is made.
iv.	Issue of TDS/TCS certificate in Form 16/16A/16B/27D	• Form 16 – by 31st May annually

Sr. No.	Particulars	Due Dates
		• Form 16B – 15 days from the due date for furnishing the challan-cum-statement.
		• Form 16A/27D – 15 days from the due date of furnishing of TDS/TCS statement.
v.	Filing in Form 15G/15H/15I for non-deduction of tax at source.	7 days from the date of receipt.
B.	**Return of Income/ Tax Audit Report/ Transfer Pricing Report**	
i.	Person covered under tax audit (other than those to whom transfer pricing is applicable)	30th September
ii.	Person covered under Transfer pricing (including those covered by domestic transfer pricing)	30th November
iii.	Other persons	Corporate assesse - 30th September, Others – 31st July.
C.	**Annual Information return**	
i.	Annual information return in case of certain specific transactions to be reported under section 285BA by specified persons.	31st August of the following year.
2.1.3	**Goods and Service Tax Compliance**	
i.	Return of outward supplies of taxable goods or services or both in Form GSTR-1	**Summary of outward supplies:** Turnover for less than INR 15 million: Quarterly return is to be filed i.e., 31 days from the end of the quarter, Turnover more than INR 15 million: 11 days from the end of the month.
ii.	Return of inward supplies of goods or services or both in Form - GSTR-2	15th of next month (suspended for now)
iii.	Regular Return in Form - GSTR-3B	20th of next month
iv.	Quarterly filing of return by composition supplier (Quarterly) in Form - GSTR-4	18th by next month of quarter end.

Sr. No.	Particulars	Due Dates
v.	Return for Non-resident taxable person in Form – GSTR-5	20th of next month
vi.	Return of Input Service Distributors GSTR-6	13th of next month
vii.	TDS Return GSTR-7	10th of next month
viii.	Return of E-commerce operator GSTR-8	10th of next month
ix.	Annual Return (Yearly) GSTR-9	31st December succeeding the end of financial year
xi.	Final Return (AT cancellation)	Within 3 months of later of cancellation or order of cancellation order

Sr. No.	Particulars	Relevant Provisions	Relevant Form	Due Dates
2.1.4 Labour Law Compliances				
i.	As per The Factories Act, every establishment shall file Consolidated annual return on yearly basis.	Section 110		On or before the 1st February following the end of the year to which it relates.
ii.	Every occupier of an establishment shall maintain a register in respect of children employed or permitted to work, under The Child Labour (Prohibition And Regulation) Act 1986.	Section 11	Form A	Yearly basis but shall be retained by the employer for a period of three years.

Sr. No.	Particulars	Relevant Provisions	Relevant Form	Due Dates
iii.	Under the Inter State Migrant Workmen (Regulation of Employment and Conditions of Service) Act, 1979 every principal employer and every contractor shall maintain such registers and keep exhibited in such a manner as may be prescribed within the premises of the establishment where the inter-state migrant workmen are employed, notices in the prescribed form containing particulars about the hours or work, nature of duty and such other information as may be prescribed.	Section 23	As may be prescribed	Continual basis
iv.	Annual return under the Payment of Bonus Act, 1965	Rule 5	Form D	1st Feb following the end of the year to which it relates.
v.	Nomination Form under the Payment of Gratuity (central) Rule 1972	Rule 6(1) & (2)	Form F	Within 30 days of completion of 1 year of services.
vi.	Annual return by principal employer under The Contract Labour (Regulation & Abolition) Central Rules, 1971.	Reg 82(2)	Form 25 (in duplicate)	Submitting not later than 15th February following

Sr. No.	Particulars	Relevant Provisions	Relevant Form	Due Dates
				the end of the year to which it relates.
vii.	Half Yearly return by the contactor under The Contract Labour (Regulation & Abolition) Central Rules, 1971.	Rule 82(1)	Form 24 (in duplicate)	Submitting not later than 30 days from the close of the half year. **Note:** Half year for the purpose of this rule means "a periods of six months commencin g from 1st January, and 1st July of every year".
viii.	Under Employee's Provident Funds and Miscellaneous Provisions Act, 1952 Payment of provident fund contribution into the account.	Para 38(1)	Form ECR (filed online)	Need to file ECR within 15 days of the close of every month.
ix.	Employees State Insurance Act 1948 **Rate of Contribution** Employer 4.75% Employee 1.75%	Rule 51	As may be prescribed	Within 15 days of the month following, in which the

Sr. No.	Particulars	Relevant Provisions	Relevant Form	Due Dates
	of wage payable to employee			wages fall due.
x.	Under Equal Remuneration Act. 1976. Register of male and female workers	Section 8, Rule 6	Form D	Continual basis
xi.	Under Maternity Benefit Act, 1961, Register of female workers who have taken benefit under the Maternity Benefit Act.	Rule 16	Form N	Continual basis

Sr. No.	Particulars	Relevant Provisions	Relevant Form	Due Dates	
2.1.5 Mandatory Annual Compliances under the Companies Act, 2013					
i.	Receipt of MBP-1	184(1)	Form MBP- 1	Every Director of the Company in First meeting of the Board of Director in each Financial Year will disclose his interest in other entities.	
ii.	Annual Filings			Due date of Filing	Due Date for every Financial Year
		92	E-Form MGT-7	60 days from the conclusion of AGM	
		137	E-Form AOC-4	30 days from the conclusion of the AGM (In case of OPC within 180 days from the close of the financial year)	
iv.	Appointment of Auditor	139	Form ADT-1	15 days from the conclusion of AGM	15th October 2018
v.	Changes in Directors	149	DIR -12	To be filed within 30 days of changes, appointment, resignation of Director	

Chapter 3

DIRECT AND INDIRECT TAX

Chapter 3 Direct and Indirect Tax

India has a well-structured tax system both for direct taxes and indirect taxes. Taxes are levied by the Central Government or State Governments or both based on the powers conferred by the Constitution.

3.1 Direct Taxes

3.1.1 Introduction

Direct taxes are levied on individuals, corporate and other business entities by the Central Government.

As per the Income Tax (IT) Act, 1961, which is the primary legislation dealing with direct taxes in India, every assessee whose total income exceeds the maximum exempt limit is liable to pay this tax. The tax structure and rates are annually prescribed by the Union Budget. This tax is imposed during each assessment year, which commences on 1st April and ends on 31st March. The total income is calculated from various heads such as business and profession, house property, salaries, capital gains, and other sources. The assesses are classified as individuals, Hindu Undivided Family (HUF), association of persons (AOP), body of individuals (BOI), company, firm (partnership firms / LLP), local authority, and artificial judicial person not falling in any other category. Under the ITAct, residents are subject to tax in India on their worldwide income, whereas non-residents are taxed only on Indian source income.India sourced income refers to income that accrues or arises in India, is deemed to accrue or arise in India or which is received or is deemed to be received in India.

3.1.2 Revenue Recognition under the IT Act

Section 9 of ITA, deems certain income of non-residents to be Indian source income. Under section 9(1), "capital gains" are considered to have their source in India and are taxable in India if they arise directly or indirectly, through the transfer of a capital asset situated in India. Similarly, the "business income" of a non-resident is taxable in India only if it accrues or arises, directly or indirectly, through or from any business connection in India. The term "business connection" is wider than "permanent establishment" which is defined in most of the Double Taxation

Avoidance Agreements. The "business connection" or "permanent establishment" can result from the presence of dependent agent who has authority to conclude contracts or who habitually secures business or due to fixed place of business or construction site exceeding certain duration or performance of services. As per the recent amendments in section 9(1)(i), a systematic and continuous soliciting of business activities or engaging in interaction with such number of users as may be prescribed, in India through digital means can create a 'business connection' for non-resident in India. This is in line with the recent OECD pronouncements for taxation of businesses based on digital presence and Base Erosion Profits Shifting (BEPS). The threshold limits are yet to be notified by the government.

Section 90(2) of the ITA is a beneficial provision which states that, where the taxpayer is situated in a country with which India has a double tax avoidance agreement ("Indian Tax Treaty"), the provisions of the ITA apply only to the extent that they are more beneficial to the taxpayer. Rules under Indian Tax Treaties are generally more beneficial to the taxpayer than those under domestic law (ITA) and hence it is typically advantageous for a non-resident taxpayer to avail treaty rates.

Certain income and expenditure which commonly arise in Pharmaceutical industries are explained below:

- **Income from Development Agreements**

  - There are cases where pharmaceutical companies enter into development agreements with Multinational Companies for development of generic formulations whose patent is expected to expire shortly. As a consideration for the development activities, the company sometimes agrees a lumpsum amount to be received on achievement of various milestones. The milestones are linked to various services to be provided by the company.

  - The company receives proportion of total consideration as upfront consideration for transfer of marketing rights to the customer. As per IND-AS 115, proportionate completion method – Performance

consists of the execution of more than one act. Revenue is recognized proportionately by reference to the performance of each act. The revenue recognized under this method would be determined on the basis of contract value, associated costs, number of acts or other suitable basis.

- Where the milestone amount is contingent to US FDA approval or any other regulatory approval as per IND-AS 37 "Contingent Asset is a possible asset that arises from past events the existence of which will be confirmed only by the occurrence or non-occurrence of one or more uncertain future events not wholly within the control of the enterprise. An enterprise should not recognize contingent asset.

– Income from Profit Share

- Pharmaceutical companies from time to time enter into marketing arrangements with various business partners for the sale of its products in certain markets. Under such arrangements, the Company sells its products to the business partners at a non-refundable base purchase price agreed upon in the arrangement and is also entitled to a profit share which is over and above the base purchase price. The profit share is typically dependent on the business partner's ultimate net sale proceeds or net profits, subject to any reductions or adjustments that are required by the terms of the arrangement.

- Revenue from such transactions should be recognized when the requirement as to performance set out in IND-AS 115 are satisfied, provided that at the time of performance it is not unnecessary to except ultimate collection, if it is not unreasonable to except ultimate collection then revenue recognition should be postponed.

- IND-AS 115 requires an entity to consider the terms of the contract and its customary business practices to determine the transaction price. The transaction price is the amount of consideration to which an entity expects to be entitled in exchange for transferring

promised goods or services to a customer. The consideration promised in a contract with a customer may include fixed amounts, variable amounts, or both. Under IND – AS, the company will have to estimate the sales by business partners and accrue for share of profit at the time of sale itself.

– Research and Development Cost

Ind AS 38 has given guidance in accounting for R&D expenditure as under:

- Research is original and planned investigation undertaken with the intention of gaining new scientific or technical knowledge and understanding – **capitalization is prohibited.**
- Development is the application of research findings or other knowledge to a plan or design for the production of new or substantially improved materials, fixtures, products, processes, system or services before the start of commercial production or use – **capitalization is required.**
- Research and development in pharmaceutical industry primarily includes in house research and development. The cost of in-house development activities are recognized as an internally generated intangible asset from the date on which all the criteria for the asset's recognition are met. An intangible asset shall be recognized if it is probable that the expected future economic benefit that are attributable to the asset will flow to the entity and the cost of the asset can be measured reliably. Generally, final regulatory approval provides substantial evidence at which point, all the criteria for capitalizations of in-house R&D cost of intangible assets have been met.
- The cost of an internally generated intangible asset comprises all directly attributable costs necessary to create, produce, and prepare the asset to be capable of operating in the manner intended by management.

3.1.3 Taxes Applicable to Companies

i. Domestic Companies

"Domestic company" means an Indian company, or any other company which, in respect of its income liable to tax under this Act, has made the prescribed arrangements for the declaration and payment, within India, of the dividends (including dividends on preference shares) payable out of such income. An Indian company means a company registered under the Companies Act 2013 or the earlier company law regulations in India. Indian companies are treated as tax resident and foreign companies are treated as tax resident if they are wholly controlled and managed from India.

Corporate tax is levied on the global earnings of resident companies. This takes into account income earned by the company outside India.

ii. Foreign Companies

A foreign company means a company which is not a domestic company. The basic taxation structure for a foreign company is as under:

Foreign company	Tax rate for FY 2018–19
Having total income exceeding INR 10crores (INR 100 million)	43.68% [(tax rate 40% plus surcharge 5% thereon) plus health and education cess 4%thereon]
Having total income exceeding INR 1,00,00,000 but not exceeding INR 10,00,00,000	42.432% [(tax rate 40% plus surcharge 2% thereon) plus health and education cess 4%thereon]
Having total income uptoINR1,00,00,000	41.60% (tax rate 40% plus health and education cess 4%thereon)

Marginal relief is available to ensure that the additional income-tax payable, including surcharge of 2% on the excess of income over INR 1,00,00,000, is limited to the amount by which the income is more than INR 1,00,00,000.

Similarly, marginal relief is available to ensure that the additional income-tax payable, including surcharge of 5% on the excess of income over INR10,00,00,000, is limited to the amount by which the income is more than INR10,00,00,000. However, no marginal relief shall be available in respect of the health and education cess.

iii. Dividend Distribution Tax (DDT)

- Dividend distribution tax is tax paid by domestic companies on the dividend that they pay to their shareholders. The effective DDT rate for FY 2018-19 is: 20.5553% [(tax rate 15% plus surcharge 12% thereon) plus health and education cess 4% thereon considering the grossing up provisions.]

- However, rate of Dividend Distribution Tax (DDT) may not be limited to dividend rate as given in Dividend Article of the DTAA since DDT is a tax levied on the company distributing the dividend and not a withholding tax deducted from the dividends. In other words, DDT does not come under the purview of Article on Dividend of the treaty, so as to apply the DDT rate as given in DTAA.

- This question was raised in Mumbai ITAT in case of **SGS India (P.) Ltd. — 83 taxmann.com 163**, as to whether the rate of DDT as prescribed in the Act can be limited to the rate as specified in the tax treaty, however, the matter was remanded back for deeper examination and no conclusion was pronounced on it. In order that Dividend rate as per DTAA is applicable , one has to first see that whether DDT is tax on the company or is the company paying DDT on behalf of shareholder. **Bombay HC in case of Godrej and Boyce** well pronounced that it is the tax on the company and Article 10 of the relevant treaty is designed to cover the dividends that are taxed in hands of the shareholder.

iv. Minimum Alternate Tax

- From AY 2012-13, where the income-tax payable by a company on

its total income is less than 18.5% of its book profit, then such book profit shall be deemed to be the total income of the assessee and the tax payable would be calculated @ 18.5% of such deemed income.

- This income tax is further increased by surcharge (as applicable) and health and education cess. MAT is applicable to all companies including foreign companies.

  1) Thus, every company has to compute its income tax liability as per two sets of provisions of Income Tax Act as follows:Income tax computed as per normal provisions of Income Tax Act.

  2) Income tax computed as per provision of section 115JB of Income Tax Act.

- **MAT Credit**

  When any amount of tax is paid as MAT by a company, then credit in respect of tax so paid shall be allowed to it in accordance with the provision of section 115JAA.

  1) Allowable Tax Credit = Difference of MAT paid and income tax payable under normal provision of Income tax Act, 1961.(However, no interest shall be paid on this Tax credit by the revenue.)

  2) Such tax credit shall be carry forward for 15 assessment years immediately succeeding the assessment year in which such credit is become allowable.

  3) Tax credit shall be allowed set off in a year when tax becomes payable on the total income in accordance with the normal provisions of the Act.

  4) Set off shall be allowed to the extent of difference between

tax on the total income (under normal provision) and tax which would have been payable u/s 115JB for that assessment year.

v. Tax Rates

Assessee	Income Tax Rate	MAT Rate	Dividend Distribution Rate*
Domestic Company	30% #	18.5%	15% (Grossed up)
Foreign Company	40%	18.5%	–

*Exclusive of Health education cess & surcharge

Tax rate is 25% (exclusive of surcharge and Health education cess) if a turnover or gross receipt of the company doesnot exceed INR 250 Crores.

Applicability of Surcharge & Education Cess:

Particulars	Applicable to Companies		A.Y. 2018–19 /2019–20	
Surcharge (as a percentage of tax rate)	Total Income	<INR 1 cr	All	NIL
		Rs 1 cr to 10 cr	Domestic	7%
			Foreign	2%
		>INR 10 cr	Domestic	12%
			Foreign	5%
Health Education Cess (as a percentage of tax rate plus surcharge)				4%

vi. Tax Deducted At Source (TDS)

As per the IT Act, any company or person making certain types of payment(such as salaries, rent, interest, contract for work, brokerage, commission and payments to resident or non-residents having income chargeable to tax in India) is required to deduct tax at source and deposit the same with the government if the payment exceeds certain threshold limits. TDS has to be deducted at the rates prescribed by the tax department.

TDS is deducted irrespective of the mode of payment—cash, cheque or credit—and is linked to the PAN of the deductor and deductee.

Disallowance Under section 40(a)(ia) of the Act

In case of payments made to resident, the deductor is allowed to claim deduction for payments as expenditure in the previous year of payment, if tax is deducted during the previous year and the same is paid on or before the due date specified for filing of return of income under section 139(1) of the Act. In case of non-deduction or non-payment of tax deducted at source (TDS) from certain payments made to residents, then 30% of the amount of expenditure on which tax was deductible is disallowed under section 40(a)(ia) for the purposes of computing income under the head "Profits and gains of business or profession".

However, if the recipient of the income furnishes his income tax return before due date taking into account such income on which the payer has not deducted tax and pays the tax on the same income, then payer is still eligible to take the deduction of such payment made to payee (recipient) in that year itself on which the tax was not deducted at source, subject to certain conditions.

vii. Withholding Tax on Certain Foreign Payments

Income of a non-resident shall be deemed to accrue or arise in India being interest, royalty and technical service and shall be included in the total income of the non-resident, whether or not-

- the non-resident has a residence or place of business or business connection in India; or
- The non-resident has rendered services in India.

a. Interest under sec. 9(1)(v) –

Interest payable by Indian resident to a non-resident on foreign

currency denominated loans attracts (referred to as External Commercial Borrowings) withholding of tax at the rate of 5% as per the provisions of the IT Act, subject to certain conditions. Further, such interest paid is a tax-deductible expense for the Indian company, if the applicable tax has been withheld before making the payments to the non-resident.

Withholding tax is applicable on Interest, if payable by:-

- the Government, both Central or State
- resident person, except where the interest pertains to any debt incurred or moneys borrowed and used for the purposes of business or profession carried on by such person outside India or for the purpose of making or earning any income from any source outside India
- a non-resident where interest pertains to any debt incurred or moneys borrowed and used for the purpose of a business or profession carried on by such person in India

b. Royalties / Fees for technical services

Payments towards Royalty and Fees for Technical Services (FTS) currently attract a withholding tax at the rate of 10% (plus surcharge as applicable) as per the provisions of the ITA on gross amount. Further, where royalties or FTS is paid to a foreign company and is effectively connected to a PE of the foreign company in India, then such payments would be taxed as business profits on "net income" basis.

Royalty means consideration (including any lump sum consideration but excluding any consideration which would be the income of the recipient chargeable under the head "Capital gains") for transfer of rights w.r.t intellectual property, imparting information concerning use of such intellectual property, imparting information concerning the use or right to

use industrial, commercial, scientific knowledge or skill , transfer of rights in respect of copyright, literary or artistic or scientific work including films or video tapes for use in connection with radio broadcasting and any service related to all the abovementioned activities.

Fees for technical services

Section 9(1)(vii) of the Act defines Fees for Technical services(FTS)as any consideration (including any lump sum consideration) for the rendering of any managerial, technical or consultancy services (including the provision of services of technical or other personnel) but does not include consideration for any construction, assembly, mining or like project undertaken by the recipient or consideration which is chargeable under the head "Salaries".

Disallowance Under section 40(a)(i) of the Act

In case of any amount payable by an assessee outside India or to non-resident in India being interest, royalty or fees for technical services on which tax at source needs to be deducted but has not been so deducted or after deduction, tax has not been paid on or before due date for filing return of income under Section 139(1), then entire such amount shall be disallowed while computing income under the head "Profits and gains from business and profession."

Lower Withholding Rate Under DTAA

- Section 90(2) of ITA, 1961 allows a non-resident taxpayer to opt between provisions of ITA and Articles of DTAAs, whichever is beneficial to the taxpayer. Also it should be noted that in order to avail the benefits of DTAAs, requirement of PAN has been relaxed, subject to other specified compliances under section 90, as mentioned below
    - Tax Residency Certificate (TRC) issued by home country of the non-resident

- Declaration in Form 10F (if required) as prescribed by Income-tax Rules and
- Self-declaration by non-resident in relation to permanent establishment in India in terms of the relevant DTAA. However it should be noted that, once the tax is withheld under the provisions of Section 206AA due to absence of PAN, then such non-resident would be unable to seek refund of excess tax withheld, on grounds of beneficial treatment of DTAA, in the assessment by filing tax returns because a non-resident is not entitled to file tax returns without having a PAN number. However, as an alternative, in such situation, taxpayer ideally can also claim Foreign Tax Credit for the portion of taxes that becomes payable under DTAA.

viii. Foreign Tax Credit (FTC)

In many countries, detailed rules on credit for foreign tax already exist in their domestic laws, which describe the computation of foreign tax credit under various circumstances. Recently India has also come out with Rules on FTC.

As per the said Rules, resident in India shall be allowed a credit for the amount of any foreign tax paid by them abroad in the year in which income corresponding to such tax has been offered to tax in India. However, where income has been offered to tax in more than one year, foreign tax credit shall be allowed across those years proportionately.

Rules provide that FTC shall not be available against any sum payable by way of Interest, Fee or Penalty. In respect of disputed Foreign Tax credit, it provides that no credit of foreign tax (part or full) which is disputed in any manner shall be available except in certain cases subject to some conditions.

The credit of foreign tax shall be the aggregate of amounts of credit

computed separately for each source of income arising from a particular country or specified territory. The amount of foreign tax Credit shall be the lower of the two:

- Tax payable under the Act on such income or
- The foreign tax paid on such income

It has been clarified that FTC shall also be available against MAT / AMT.

Further, the rules provides for furnishing of certain specified documentation for availing FTC.

For countries with no DTAAs with India, a unilateral tax credit for tax paid in foreign countries is available under Indian domestic law to a resident tax payer.

ix. Capital Gains

Capital gains tax is a tax that is charged on the profits that have been made on the sale of capital assets. Under IT Act, the capital assets are treated as 'Short-Term Capital Asset and 'Long-Term Capital Asset'.

- Short-term capital assets (Shares / Securities): Shares and securities that are held by the taxpayer for a period not more than 12 months preceding the date of its transfer,
- Long-term capital assets (Shares / Securities): Shares / securities that are held for a period exceeding 12 months before the transfer are treated as long-term assets.
    - Shares & securities includes equity shares which are listed on a recognised stock exchange, units of equity oriented mutual funds, listed debentures and Government securities, units of UTI and Zero Coupon Bonds. Transfer can be termed as giving up right on an asset which includes sale, exchange, and

compulsory acquisition under any law and relinquishment.

These gains are taxed as follows:

- Long-term capital gains arising on transfer of listed equity shares (including units of an equity oriented fund and units of business trust) on a recognized stock exchange in India if:

  - Sale of shares before 31st March 2018, then the long term capital gains are exempted in the hands of the taxpayer u/s 10(38), it may be noted that since long term capital gains are exempted, long term capital loss shall have no tax treatment and such long term capital loss can neither be set off against any income nor be carried forward.

  - Long term capital gains in excess of Rs. 1 lakh arising on sale of shares after 1st April 2018, is chargeable u/s 112A in the hands of the taxpayer @ 10% on shares held for more than 12 months irrespective of the date of purchase

  - However, relief is provided in respect of grandfathering of long term capital gains upto 31 January 2018 and gains after that period in respect of equity shares sold on or after 1 April 2018, shall be taxable under the new rate of 10%, if sold on recognized stock exchange and securities transaction tax is paid thereon. The gains from equity share held up to one year will remain short term capital gain and will continue to be taxed at the rate of 15% (if sold on recognized stock exchange and securities transaction tax is paid thereon). However, the period of holding will be considered from the date of original investment and not from January 31, 2018.

  - Capital gains realized on sale of unlisted Indian securities would be taxed at the rate of 20% for long-term gains and as normal income in case of short-term gains.

- The benefit of exemption from long term capital gains u/s 10(38) and lower tax rate of 15% on short term capital gains on transfer of equity shares could be availed only if securities transaction tax had been paid on transfer. However, it is important to note that the above capital gains arising to non-resident on selling of Indian company's shares, which were earlier exempted under various DTAA such as India- Singapore DTAA, India-Mauritius DTAA and India-Cyprus DTAA, is now made taxable by amending those DTAA, subject to the grandfathering provisions under the treaty.

3.1.4 Incentives under the IT Act

The term Scientific Research has been defined as 'an activity for the extension of knowledge in the fields of natural or applied sciences. In order to encourage people to innovate, the government has provided certain tax incentives under Income Tax Act for various sectors, including the pharmaceuticals sector by way of deduction for expenditure incurred on Scientific Research. Such deductions can be claimed by carrying out In-house scientific research or by contributing to outside agencies engaged in scientific research, conducting clinical trials, developing new drug molecules etc.

– In-House Research and Development

- The company should engage in the business of bio-technology or in any business of manufacture or production of any article or thing except those specified in the Eleventh Schedule.
- The expenditure on scientific research in relation to drugs and pharmaceuticals shall include expenditure incurred on clinical drug trial, regulatory approval and filing an application for a patent. Even capital expenditure incurred on lab equipment's and computer used for purpose of clinical trials is eligible for allowance under section 35(2AB).

- Deduction shall be allowed if the company enters into an agreement with the prescribed authority for cooperation in such research and development facility and fulfills prescribed conditions with regard to maintenance and audit of accounts and also furnishes prescribed reports. Such report is to be submitted to Principal Chief Commissioner or Chief Commissioner having jurisdiction over the company claiming the deduction under this section.

  Amount of deduction – If all above conditions are satisfied, the quantum of deduction is as follows –

For the Assessment Year 2018–19 to 2020–21	150% of actual expenditure
For the Assessment Year 2021–22 onwards	100% of actual expenditure

– **Contributions Made to Other Institutions for Scientific Research**

Where the assessee does not himself carry on research but makes contribution to the following institutions for the purpose, a deduction is allowed as follows:

To whom contribution can be given	Deduction (as a percentage of actual expenditure)	
	For A.Ys 2018–19 to 2020–21	For A.Ys 2018–19 to 2020–21
An approved scientific association which has, as its object, undertaking of scientific research related or unrelated to the business of assessee	150%	100%
An approved university, college or other institution for the use of scientific research related or unrelated to the business of assessee [sec. 35(1)(ii)]	150%	100%

To whom contribution can be given	Deduction (as a percentage of actual expenditure)	
	For A.Ys 2018–19 to 2020–21	For A.Ys 2018–19 to 2020–21
An approved university, college or other institution for the use of research in social sciences or statistical research related or unrelated to the business of the assessee [sec.35(1)(iii)	100%	100%

- **Capital Expenditure Incurred by an Assessee Carrying on Scientific Research**

Where the assessee incurs any expenditure of a capital nature on scientific research related to his business, the whole of such expenditure incurred in any previous year is allowable as deduction for that previous year.

The three ingredients necessary to be satisfied for allowance under section 35 are:

a) that the expenditure has been incurred during the year;

b) that it is of capital nature; and

c) that it is on scientific research.

Pre-commencement period expenses: Where any expenditure has been incurred on scientific research related to business before the commencement of the business, the aggregate of such expenditure, incurred within the three years immediately preceding the commencement of the business, is deductible in the previous year in which the business is commenced [Explanation to section 35(2)(ia)].

- **Incentives to Venture Capital Funds**

In order to encourage investment by venture capitalists, the IT Act has

granted certain tax incentives to Venture Capital Funds (VCF) registered with the Securities and Exchange Board of India (SEBI) which invest into certain pharmaceutical businesses. Thus exemption is provided for income earned by VCF arising from investment in pharmaceutical companies engaged in "bio-technology" and "research and development of new chemical entities in pharmaceutical sector". However, such income becomes taxable upon distribution.

3.1.5 Potential Permanent Establishment Issues in Contract Research and Manufacturing

The research and manufacture outsourcing arrangement entered into by foreign enterprise with Indian CRO/ CMO shall invite the risk of the Indian counterpart being regarded as permanent establishment and consequently lead to enhanced tax burden by way of tax on global income at rate of 40%, unless the transaction can be demonstrated to be at arm's length. Also, business income of non-resident arising from a business connection in India shall be taxed at rate of 40% with respect to income attributable to PE in India. The term 'business connection' under IT Act, 1961 has very wide definition which has been evidenced by court judgements in the past as compared to the definition of 'PE' in tax treaties. Nevertheless, the tax payer can avail of the tax treaty provisions, if the same is beneficial to them, subject to certain compliances as specified under the Income Tax Act.

- **Fixed Place of Business PE**

  - If the business of foreign enterprise is, wholly or partly, carried on through a fixed place of business in India, then such foreign enterprise is deemed to have a PE in India.

  - In case of contract research and manufacturing being outsourced by foreign enterprise to Indian CRO/ CMO, the said outsourcing arrangement could constitute fixed place of business PE on the basis of cumulative satisfaction of three tests as under:

a. **Disposal test** – When some structure present in India is at disposal of non-resident then this test is satisfied;

b. **Permanence test** - When any fixed structure like buildings, machines, etc. of non-resident is present permanently in India. It does not require the assets to be affixed to the ground and mere keeping the machine as it is on permanent basis can satisfy this test.

Place of business – Non-resident should be carrying out business from such fixed place to satisfy this test

- Usually, outsourcing of contract research and manufacturing requires the foreign enterprise to send their personnel for a reasonable period of time to carry out training, supervision and inspection activities at the premises of Indian CRO/ CMO to ensure standardization. In such cases the desk allotted to the employees of the foreign enterprise could be considered as "fixed place of business" though the place is not owned or rented by the foreign entity. In most of the treaties, under the provisions of Article 5, for construction or supervisory activities deputation of personnel for a limited period (say less than 6 months, etc) shall not have a PE implication. Thus, such arrangements need to be carefully analysed to understand PE implication in India.

– Service PE

- Under certain Indian Tax Treaties, rendering of services by employees of non-resident enterprise over a specific period of time may be considered as Service PE. E.g. under the India-US tax treaty, a PE is said to be constituted where there is:

"(i) the furnishing of services, other than included services as defined in article 12 (royalties and fees for included services), within a Contracting State by an enterprise through employees or other

personnel, but only if:

- activities of that nature continue within that State for a period or periods aggregating to more than 90 days within any 12 month period; or
- The services are performed within that State for a related enterprise (within the meaning of paragraph 1 of article 9 (associated enterprises)).

- Thus, the training and inspection services provided by personnel of foreign enterprises to India CRO/ CMO beyond prescribed time limit might constitute Service PE considering provisions of applicable DTAAs.

– **Agency PE**

- According to Indian tax treaties, if the Indian counterpart of foreign enterprise, has and habitually exercises an authority to conclude contracts on behalf of the foreign enterprise,then such Indian entity may be treated as a PE of a foreign enterprise.

- Though most of the contract manufacturing arrangements with India CMO are structured in such a way wherein the right to represent foreign enterprise in negotiations is not granted to Indian entity, such an arrangement might attract PE provisions on the basis of the Indian entity maintaining and delivering final pharmaceutical product on behalf of foreign enterprise or playing a significant role in concluding the contracts.

- Outsourcing of research and manufacturing functions by foreign entity to its Indian subsidiary (Indian CRO/ CMO) does not by itself constitute PE of the foreign entity in India as far as the subsidiary functions independently.

Constitution of PE of foreign entity in India depends on the

structuring of the arrangement and shall be decided according to facts and circumstances of each case.

- **Issue of Taxation as an Association of Persons**

  - In some cases research and manufacturing functions are based on revenue sharing model with foreign enterprise being entrusted with the responsibility of co- developing drugs with Indian CRO/ CMO. Such an arrangement could be taxed as an association of person "AOP" at maximum marginal rate (in absence of PE in India). The arrangement shall be structured so as to avoid 'common activities object' which is essential for taxation of AOP in India and the contract manufacturing shall be undertaken independently, on contract basis.

3.1.6 Place of Effective Management (POEM)

- **POEM: Explanation to Section 6(3)**

"For the purposes of this clause "place of effective management' means a place where key management and commercial decisions that are necessary for the conduct of the business of an entity as a whole are, in substance made."

- **POEM Guidelines**

  CBDT Circular No.8 of 2017 – POEM provisions in section 6(3) not to apply to a foreign company having turnover or gross receipts < = INR50 crores in a financial year.

- **Two Broad Categories**

  I) Company engaged in active business outside India

  ii) Other than company engaged in active business outside India

- **Active business outside India**

  Satisfaction of Cumulative conditions as follows:

I) If passive income <= 50% of its total income

ii) Less than 50% of total assets situated in India

iii) Less than 50% of total number of employees situated in India or resident in India

iv) Payroll expenses on such employees < 50% of total payroll expenses.

Thus, average of 3 years data is important. If tax accounting year is different from previous year, then data of accounting year ending in previous year.

- **If engaged in active business outside India**
  - **If majority meetings of Board of Directors (BoD) outside India – POEM presumed outside India**
  - However, if BoD standing aside i.e. powers of management are exercised by the Holding Company or any other person resident in India – POEM in India
  - Merely because BoD follows general and objective principles of global policy – can't be said to be standing aside.
- **If not engaged in active business outside India**
  - **Two stage process:**
  - **First** – identification or ascertaining of person(s) actually making key management and commercial decisions
  - **Second** – determination of place where these decisions are made.

Thus, Place of Decisions more important than place of implementation. Active business outside India needs to be decided

based on certain guiding principles prescribed under the IT Act, 1961.

- **Secondary factors (to be considered if the 'active business outside India test' does not lead to clear identification of POEM)**
  - Place of main and substantial activity OR
  - Place of accounting records

The final guidelines specify that the following aspects need to be kept in mind while deciding POEM:

- Facts and circumstances of each case
- Concept of substance over form
- No single principle is decisive in itself and the principles are to be seen with regard to activities performed over a period of time rather than any particular point moment in time

– **Procedural Aspects**

- Initiating any proceedings for holding POEM – AO needs to seek prior approval of Prin. Commissioner or Commissioner
- Holding POEM – AO needs to seek prior approval of the collegium of three members consisting of Prin. Commissioners or Commissioners – opportunity of being heard to be given.

– **Poem In International Tax Treaties**

- Article 4(3) – Residence
  - Dual residence – Tie-breaker rule applicable
  - As per tie-breaker rule, company is deemed to be resident of the contracting state where Place of Effective management is situated

- If POEM is difficult to be determined, then Tax Treaty suggests Mutual Agreement Procedure ('MAP') route to determine the tax residence of a corporate entity

- **Illustrative* List of Countries – Tie Breaker Test for Residency**

Sr. No.	Criteria	Countries*
1	Place of Effective Management	Japan, Singapore, Mauritius, UK
2	Competent Authorities	Canada
3	No Tie-breaker test -– Double taxation	US
4	Residency - where its Head Office is situated	China
5	Control and Management	Greece

– **Possible Implications of Poem in India**

- Foreign Company becomes a resident in India
- Tax rate of 40% applicable
- Worldwide income taxable
- Concessional rates of tax under section 112 or section 115A continue
- Treaty available – though the other country is likely to become a source state – at times could be beneficial

3.1.7 Indian Transfer Pricing Issues in Contract Research and Manufacturing

– The entities which are looking for outsourcing research and manufacturing functions to an associated enterprise, such as in cases of captive outsourcing, the fees payable to the such service provider should take into account transfer pricing regulations as applicable in India.

– The basic rule contained in the Transfer Pricing Regulations is that any

income arising from an ''international transaction''shall be computed having regard to the arm's length price. The Transfer Pricing Regulations define ''associated enterprise'' to include any enterprise that participates directly or indirectly or through one or more intermediaries in the management or control or capital of another enterprise. Enterprises may also be regarded as ''associated'' by virtue of borrowings, guarantees, licensing of trademarks, purchase, sales or where enterprises have ''mutual interest'' as may be prescribed by the revenue authorities. Here, ''enterprise'' is defined broadly and covers any entity (including a permanent establishment) which engages in any activity relating to the provision of goods / services of any kind, investment activity, dealing in securities and extending loans. The term ''international transaction'' has been defined as a transaction between two or more associated enterprises, either or both of which are non-residents.

– Arm's Length Price

- Arm's length price can be termed as the price which is applied or proposed to be applied in a transaction between persons other than associated enterprises, in uncontrolled conditions. The OECD Transfer Pricing Guidelines for Multinational Enterprises and Tax Administrations, 2010 (''Guidelines'') provide that the application of the arm's length principle is generally based on a comparison of all the relevant conditions in a controlled transaction with the conditions in an uncontrolled transaction. As per the Guidelines, comparability of the transactions can be achieved only when there are no differences in the conditions that could materially affect the price or when reasonably accurate adjustments can be made to eliminate the effects of any such differences. The comparative analysis of the controlled transactions with uncontrolled transactions is the basic requirement of ascertaining whether the controlled transactions adhere to the arm's length standard.

- Where arm's length price is within 3% range of the transaction price,

no adjustment is warranted but if it is beyond 3% range, adjustment is required to be made to the transfer price and benefit of tolerance range is not available. The arm's length price in relation to an international transaction is to be determined by any of the following methods depending on which is most appropriate for the enterprises:

- Comparable uncontrolled price method;
- Resale price method;
- Cost plus method;
- Profit split method;
- Transactional net margin method;

- Such other method that may be prescribed by the Central Board of Direct Taxes (till date, no other method that may be considered appropriate in determining the arm's length price has been prescribed).
- The pharmaceutical industry in India also faces issues pertaining to arriving at a comparable arm's length price for the purpose of transfer pricing.
- If there are two or more appropriate prices assumed for a certain transaction, the arm's length price will be calculated as the average of the prices.
- At the end of a financial year, the person or group involved in an international transaction should submit the report of Chartered Accountant in Form 3CEB .
- This form has to be filed along with the Income Tax return of the same period.

- **Specified Domestic Transaction (SDT) – TP Regulations**

The scope of TP was widened from FY 2012-13 by extending the same to be Specified Domestic Transactions (SDT). As per Section 92BA which defines SDT is amended vide Finance Act 2017 and has removed expenditure incurred for undertaking transactions with related parties as specified in Section 40A(2)(b). The said amendment is applicable from assessment year 2017-18. Section 92BA defines SDT which is covered by TP regulations as under:

i.) Any transactions referred to in section 80A;

ii.) Any transfer of goods or services referred in sub-section (8) of the section 80-IA;

iii.) Any business transacted between the Assessee and other person as referred to in sub-section (10) of section 80-IA;

iv.) Any transaction, referred to in any other section under Chapter VI-A or section 10AA, to which provisions of sub-section (8) or sub-section (10) of section 80-IA are applicable.

- **Threshold Limit and Coverage**

  All the transactions covered under the above 5 limbs of section 92BA will be regarded as SDT only if the aggregate value of all transactions in the previous year exceeds the threshold limit of INR 20 Crores (INR 200 million). If any of the above mentioned SDT crosses the threshold limit of INR 20 Crores , TP compliances would be applicable for all such transactions.

3.1.8 Country-By-Country Reporting and Furnishing of Master File

With a view to align the existing Indian Transfer Pricing regulations pertaining to maintenance of documentation, the Finance Act, 2016 adopted Action 13 of the Action Plan on BEPS ('BEPS Action Plan 13') for Transfer Pricing Documentation

and Country-By-Country Reporting ('CbCR') by introducing an amendment to section 92D and inserting a new section 286 to the Act. These provisions require an international group to provide description of the transfer pricing policies regarding intangibles, R&D and financing arrangements and are effective from AY 2017-18 (financial year commencing from 1st April 2016) and subsequent assessment years. Further, CBDT on 31st October 2017 issued a notification with respect to the new Rules 10DA, 10DB and new Forms namely Form no. 3CEAA to Form No. 3CEAE for laying down the guidelines for maintaining and furnishing of transfer pricing.

Following are the conditions related to applicability of CbCR/Master File:

Particulars	Forms as prescribed by CBDT	Due Dates
Required ***to be filed by every constituent entity (resident and non-resident entity)*** of an international group whether or not it satisfies the cumulative conditions as prescribed by CBDT	Part A of Form No. 3CEAA	30 November 2018
Required to be filed ***only by those constituent entity(s)*** which satisfies both the cumulatively conditions as prescribed by CBDT. The same has been reproduced as below: Consolidated group revenue for the accounting year exceeds INR 500 crores (INR 5 billion) (i.e. approx. USD 76.83 million*); **AND** The aggregate value of international transactions as per books of accounts, for the accounting year exceeds INR 50 crores (INR 500 million) (approx. USD 7.68 million*) **OR** Purchase, sale, transfer, lease or use of intangible property exceeds INR 10 crores (INR 100 million) (approx. USD 1.54 million*)	Part B of Form No. 3CEAA	30 November 2018

Particulars	Forms as prescribed by CBDT	Due Dates
Where there are more than 1 constituent entities resident in India of the international group, the international group has to designate a constituent Indian entity to file Master File and the ***intimation has to be filed by that designated constituent entity*** in relevant form	Form No. 3CEAB	31 October 2018
Every constituent entity **resident in India** where its parent entity is **not resident in India** shall intimate the Director General of Income-tax (Risk Assessment) (a) whether it is the alternate reporting entity or (b) the details of the parent entity or the alternate reporting entity, who will file CbCR in Form No. 3CEAD. The intimation shall be made at ***least 2 months prior to the due date for furnishing CbCR i.e. within 12 months from the end of the reporting accounting year.***	Form No. 3CEAC	31 October 2018
CbCR is required to be furnished in case ***total consolidated group revenue of the accounting year preceding the reporting accounting year of the international group exceeds the threshold limit of INR 5,500 crores*** (INR 55,000 million) (i.e. approx. USD 810 million*)	Form No. 3CEAD	31 December 2018 #(Refer Note No.1)
If there are ***more than one constituent entities resident in India*** of an international group, then CbCR may be furnished by that entity ***which has been designated by the international group*** to furnish the said report and the same has been intimated to the Director General of Income-tax (Risk Assessment) in relevant form	Form No. 3CEAE	Due date to be notified by CBDT

*(Exchange rate considered as on 31 March 2018 i.e. USD 1 = INR 65.0746)

#Note No. 1: If an alternate reporting entity of the international group has furnished CbCR with the tax authority of the country in which such entity is resident on or

before the date specified by that country then filing of CbCR is not required in India subject to following conditions are satisfied, namely:—

(a) the report is required to be furnished under the law for the time being in force in the said country or territory;

(b) the said country or territory has entered into an agreement with India providing for exchange of the said report;

(c) the prescribed authority has not conveyed any systemic failure in respect of the said country or territory to any constituent entity of the group that is resident in India;

(d) the said country or territory has been informed in writing by the constituent entity that it is the alternate reporting entity on behalf of the international group; and

(e) the prescribed authority has been informed by the entity referred to in sub-section (4) in accordance with sub-section (1).

A. Contents of Local File

- The Local File is required along with the master file and CbCR to provide information regarding intercompany transactions which include:Local Management structure and an organization chart, and disclosure of local management reporting lines;
- Details of intercompany transactions and financial information;
- Copies of material intercompany agreements entered by local entity;
- Detailed functional and economic analysis for the intercompany transactions:
  - With preference for local comparable
  - With search for comparable companies once every three

years for same functional profile and annual data

- Details of unilateral/bilateral/multilateral APAs, and other rulings related to the transaction of the entity.
- The Local File is to be filled locally and it is recommended that it be finalized by the filing date for the local tax return.

B. Employees

- Reporting Multinational Enterprise (MNE) is required to report number of employees in CbCR. Such reporting may be made consistently on either of the following basis:
  - Average number of employees during the year (Option for following this method shall be made in the first year which shall be consistently followed in subsequent years) or
  - Any other basis.
- Further, CbCR rules provide that only the 'Resident Employees' must be considered for the purpose of reporting as part of CbCR. Hence, one must annually take stock of residential status of the employees for reporting in CbCR purpose.
- It is pertinent to note that independent contractors participating in the ordinary operating activities of the Company are required to be reported as employees.

C. Geographical Market for the Products

- The MF Rules requires list of the major geographical market for the products and services of the Group. In situations, where India is one of the major markets for the Group products or services, a detailed analysis of the functions of the Indian Company would need to undertake, as India would be considered as significant contributor to the Group value or business.

- MNC companies having entities or PE's in India doing marketing support functions could be scrutinized and higher attribution could be made to India, based on the a detailed FAR analysis. The defragmentation rules under the new PE definition could aid the tax authorities to look at the substance of the operations in a consolidated manner.

D. FAR Analysis

- An international Group is required to disclose Function, assets and risk analysis of the constituent entities of the international group that contribute at least 10% of the revenues or assets or profits of the group.

- It appears that evaluation of all these criteria is to be done at annual basis to ascertain applicability of this relevant clause. This is certainly an onerous process in case of an international group.

E. Important Business Restructuring, Acquisitions and Divestments

- The MF Rules require description of business restructuring transactions, acquisitions and divestments.

- The disclosure here is very crucial and any business restructuring under Transfer Pricing would require an arm's length determination between the impacted entities.

- While the term 'acquisition' and 'divestments' have limited connotation and easily comprehensible, the terms 'business restructuring' needs deeper understanding.

- As per OECD guidelines, it is defined as cross border re-deployment by a multinational enterprise of functions, assets and/or risks. In simpleton, change in FAR many times trigger business restructuring. It is pertinent to note that every restructuring would not constitute a

business restructuring under transfer pricing.

3.1.9 Safe Harbour Rules

In order to reduce the number of transfer pricing audits and prolonged disputes, the CBDT issued the Safe Harbour Rules ('SHR') on 18th September 2013 under Finance (No 2) Act, 2009 with retrospective effect from 1st April 2009. SHR is covered under section 92CB of the Act and the Rules are comprehended in Rules 10TA to 10TG.

A "Safe Harbour" is defined in the Act as circumstances in which the Tax Authorities shall accept the transfer price declared by the assessee. CBDT, vide notification 46/2017 dated 7th June 2017,has amended the safe harbour rules by extending the applicability to an additional category of international transactions as well revising the applicable price/margins that would be accepted as arm's length. The SHR is effective from assessment year 2017–18, i.e., relevant to the fiscal year, ended 31st March, 2017. **Key features of these rules are:**

- The Taxpayer has the option to opt for the safe harbour under the old rules or the amended rules, whichever is more beneficial.
- SHRs are applicable for a maximum period of 5 years starting from AY 2013–14 for the prescribed sectors. The option of being governed by SHRs shall continue to remain in force for the period specified by the taxpayer in the prescribed form (Form No. 3CEFA) or a period of 5 year, whichever is less.
- A taxpayer opting for SHR shall not be allowed to invoke Mutual Agreement Procedure ('MAP') provided under relevant DTAAs.
- The new safe harbour regime is available for transactions involving provision of software development services, provision of information technology–enabled services, provision of knowledge process outsourcing services, provision of contract research and development services wholly or partly relating to software development and provision of contract research and

development services wholly or partly relating to generic pharmaceutical drugs, intra-group loans denominated in foreign currency.

3.1.10 General Anti-Avoidance Rule (GAAR)

Finance Act, 2012 has introduced the provisions of GAAR in the IT Act. The question of substance over form has been consistently arising in the implementation of taxation laws. In view of the aggressive tax planning with the use of sophisticated structures and other aspects, the statutory provisions are required to codify the doctrine of 'substance over form' where the real intention of the parties and effect of transactions and purpose of an arrangement is taken into account for determining the tax consequences, irrespective of the legal structure that has been superimposed to camouflage the real intent and purpose.

Consistent with the international trend to curb tax avoidance, India introduced GAAR provision few years ago. GAAR is made effective from 1 April 2017. For the proper implementation of GAAR, it is expected that the Government will issue a Guidance Note.

GAAR is a broad set of provisions which empower tax authorities to consider an arrangement to be an impermissible tax avoidance arrangement, if it is entered with the main purpose of a tax benefit. Tax benefit includes relief claimed under the tax treaty. In case GAAR is invoked, it will override the provisions of tax treaty.

Recently, the provisions of GAAR have been amended to provided that GAAR will not be applicable to any income arising from transfer of investment made before 1 April 2017. Further, there are certain cases, where the provisions of GAAR shall not be applicable. For instance, GAAR provisions cannot be invoked where the tax benefit to all parties to the arrangement does not exceed INR 30 million.

3.1.11 Inadmissibility of Expenses Incurred in Unethical Promotion

- The Indian Medical Council (Professional Conduct, Etiquette and Ethics) Regulations, 2002 prohibit the medical practitioners and their professional associations from taking any Gift, Travel facility, Hospitality, Cash or monetary grant from the pharmaceutical and allied health sector Industries.

- Section 37(1) of ITA provides for deduction of revenue expenditure (other than those failing under section 30 to 36) from the business income if such expense is laid out/expended wholly or exclusively for the purpose of business or profession. However, the explanation appended to this subsection denies claim of any expenses, if the same has been incurred for a purpose which is either an offence or prohibited by law.

- CBDT has issued circular no. 5/2012 dated August 5, 2012 stating that any expenses incurred in providing freebies to a medical practitioner which are in violation of the Regulation shall not be admissible as a "business expenses deduction". However, the validity of this circular was questioned in Mumbai Tribunal decision (Aristo Pharmaceuticals TS-445-ITAT-2018(Mum)) and it was held that this circular incorrectly enlarged the scope by making them applicable to pharma companies. The prohibition was imposed on the medical practitioner to accept such freebies and not on the pharma companies to provide such freebies. Pharma companies by providing such freebies are not violating any statute or law, hence such freebies to medical practitioner can be allowed as business expense deduction to pharmaceutical companies as per the recent Mumbai Tribunal decision.

- It is also clarified that the sum equivalent to value of freebies enjoyed by the aforesaid medical practitioner or professional associations is taxable as their business income or income from other sources as the case may be depending on the facts of each case. The Assessing Officers of such medical practitioner or professional associations should examine the same and take an appropriate action.

- List of few inadmissible/prohibited expenses:

  - Gifts like computer / laptops / i-pads / mobile, etc.,
  - Travelling / hospitality (Foreign / domestic leisure trip; Travelling for attending conferences;
  - Hospitality

- Cash or monetary grants
- Promotional expenses, in some cases.

3.2 Indirect Taxes

3.2.1 GST: Overview

- GST is an indirect tax levied on supply of goods and/or services. [Supply includes – sale, transfer, exchange, barter, lease, rental, license or disposal made or agreed to be made for a consideration.]
- GST comprises of:
  - CGST– Central GST
  - SGST/UTGST– State/Union Territory GST
  - IGST– Integrated GST levied by Centre on inter–state transactions and shared with states.
- Registration under GST — When Aggregate turnover in FY exceeds INR 20 lakhs.

3.2.2 Taxes Subsumed Under GST

- Excise Duty (Central & Additional both)
- Central Sales Tax
- VAT
- Service Tax
- Purchase tax
- Octroi
- Entry Tax

- Luxury Tax
- CVD & SAD
- Entertainment and Amusement tax (except when levied by the local bodies)

3.2.3 GST Rates

Particulars	Pre-GST Scenario	GST Scenario
Most of Drugs	4% (VAT)	5%
Ayurvedic Medicines	4% (VAT)	12%
Medicine Supplements	12% to 15% (VAT)	18% to 28%
Raw Material (manufacturing level)	5% (VAT)	12%
Excise Duty on Pharma Products	12.5% (ED)	No Excise Duty

3.2.4 GST Audit

- As per Section 2(13) of CGST Act, 2017, GST Audit is required when turnover exceeds INR 2 Crores.
- GST Audit is to be done by a Chartered Accountant or a Cost Accountant or Tax authorities.

3.2.5 Positive Impact of GST

- The technical machineries & equipment which are imported by the healthcare centers are normally very costly. Under the VAT regime the duty paid on such imports was also not allowed as credit. However, under the GST regime, such duty paid would be allowed as credit and thereby the effective total cost of technology in Healthcare and Pharma Industries would go down.
- Interstate transactions between two dealers become tax neutral under GST regime, replacing traditional and C&F distribution mode.
- Under GST regime there is no reversal of credit set-off in case of stock transfers and no CST liability. That would result in increase in the margins of

the manufacturers.

3.2.6 Negative Impact of GST

- GST is said to increase the indirect tax paid by pharma companies by around 60% and MRP by around 4%.
- Manufacturers who were operating under Excise Free Manufacturing zones now need to pay tax under GST regime.
- The Distribution channels were not involved in tax payments and filing tax returns under old scenario. However, they are now supposed to file minimum 25 GST returns annually (although this is going to go down to 13 returns in due course).
- GST is applicable on phases of the supply chain. It has a negative impact on free-drugs samples, bonus/discount schemes, inter-state stock transfer, etc. No credit of GST paid on such goods will be allowed to be taken as the supply of such goods does not attract GST liability.
- As per the provisions related to supply, disposal of business assets without consideration is liable for GST.

3.2.7 Input Tax Credit (ITC)

- ITC can be claimed on an end-to-end basis.
- Input tax attributable to taxable supplies including zero rated supplies, used for the purpose of business.
- Where goods are received in lots or installments, ITC will be allowed to be availed when the last lot or installment is received.

Conditions for availing ITC

- Supplies should be in furtherance of business.
- Possession of Tax invoice / equivalent document

- Tax charged is actually paid to the government.

Non-eligibility to ITC

- Payment not made within 180 days from date of issue of invoice.
- No ITC after filing of returns for the month of September of succeeding financial year for the invoice pertaining to any financial year.
- If depreciation of tax component has been claimed.

Inadmissible credits as per section 17(5)

ITC shall not be available in respect of the following inward supplies:

- Motor vehicles and other conveyances except when they are used for making such supplies as defined under the Act.
- Food and beverages, outdoor catering, health service, cosmetic and plastic surgery except where such inward supply is used for making outward supply of same category.
- Membership of a club, health and fitness centre.
- Rent-a-cab, life insurance, health insurance except where the government notifies such services as an obligatory under any law.
- Travel benefits extended to employees on vacation.
- Works contract service for construction of immovable property except plant & machinery.
- Supply received for construction of immovable property on his own account.
- Supply on which tax paid under composition scheme.
- Supply used for personal consumption.

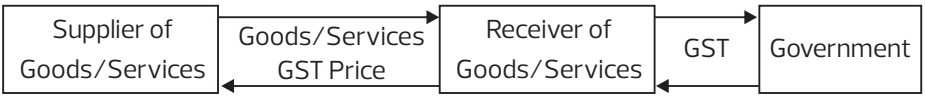
- Goods lost, stolen, destroyed, written off or disposed of by way of gift or free samples.

- Tax paid by reason of fraud or any wilful misstatements/ suppression of facts, detention, seizure and release of goods , confiscation of goods and levy of penalty.

3.2.8 Reverse Charge Mechanism

Normally, the supplier of goods or services pays the tax on supply. In the case of Reverse Charge, the receiver becomes liable to pay the tax, i.e., the chargeability gets reversed.

Payment in case of Reverse Charge



As per Section 9(4) of CGST Act, any inward supply from an unregistered person exceeding value INR 5,000 (per day for all suppliers in aggregate) shall be liable to be taxed on reverse charge basis by the recipient of such goods & services. **[Deferred till 30.09.2019 vide notification no.22/2018–Central Tax (Rate) dated 6th August, 2018]**

As per Section 9(3) of the CGST Act, following major services, inter alia, have been specified under the list of compulsory RCM: **[notification no. 22/2018 not applicable so RCM provisions not deferred]**

- Import of goods / services

- Services by a goods transport agency (GTA) in respect of transportation of goods by road @ 5%

- Services by an individual advocate or firm of advocates by way of legal services @ 18%

- Services by a director of a company or a body corporate to the said

company or the body corporate (except remuneration) @ 18%

- Sponsorship services @ 18%
- Insurance agent services @ 18% etc.

As per decision in GST Council Meeting Section 9(4) has been deferred by Government as per the notification stated above, however, section 9(3) is still applicable.

- The registered dealer who has to pay GST under reverse charge has to do self-invoicing for the purchases made.
- Payment of reverse charge liability is to be done from Cash ledger and cannot be adjusted against the input tax credit available. Input Tax Credit can be availed on taxes paid under RCM after payment of the same using balance in electronic ledger. However on certain items, no input credit is available like Food, Catering etc., while on other items input credit is available only after payment of reverse charge liability.

Payment of Consideration

If the recipient does not pay the consideration within a period of 180 days from the date of issue of the invoice, the amount of input tax credit availed proportionate to the amount of consideration not paid would be added to his output tax liability. The ITC so reversed can be reclaimed by the recipient after payment of consideration as well as the tax payable thereon. This provision is applicable to supplies with consideration.

3.2.9 Removal of Goods as Free Samples / for Quality Testing

In the non-GST scenario, finished products used for quality control or kept as sample till their expiry period were not liable for excise duty unless the same were removed outside the factory. Under GST regime, even if the same are sent out for quality test; GST may not be applicable since it does not amount to supply. However, ITC need to be reversed on goods given as free samples.

3.2.10 Return of Expired Goods

- Returns made within specified period (i.e. before end of September or filing annual return whichever is earlier):- the supplier can reduce his liability provided the recipient reverses the credit and a debit/credit note is duly issued.
- Returns made after the period (as specified above):- the supplier/chemists/stockists are required to pay the GST as the transaction amounts to Supply.
- The manufacturer will not be eligible to take the credit of GST paid on such supply in any of cases above; as the goods are to be destroyed at manufacturer's end.

CBIC has recently clarified on Goods Return (Expiry/Breakage etc.)- Circular No.72/46/2018-GST

This circular has provided two options that can be adopted in such case which are as follows:

Option A: Return of Goods to be treated as Fresh Supply

- The retailer/wholesaler/distributor returning goods back to wholesaler/manufacturers may treat this return of goods as fresh supply and issue a Tax invoice accordingly.
- Tax shall be levied separately on the tax invoice by the registered person returning the goods and reflect in its GSTR 1.
- The dealer receiving such goods shall be eligible to claim ITC on such receipt of goods.
- On destroying those goods, the manufacturer need to reverse the ITC credit as per section 17 of CGST Act.

Option B: Return of Goods by issuing credit notes

- Under GST the supplier of goods is only eligible to issue Credit note against supply.
- While receiving these goods the manufacturer/distributor/wholesaler shall issue credit note to the registered dealer who is sending back the goods.
- There is no last date for isuue of credit notes, however if the manufacturer/distributor/wholesaler wishes to levy GST on the credit note value then credit note for any FY needs to be issued and adjusted before next year September due date of filing of GST Return.
- If the credit note is issued after September return due date for the previous financial year, the tax adjustment would not be allowed and the credit note shall be issued without tax element.

3.2.11 Compliances under GST

- Every taxpayer shall apply for registration in every such state from where he makes a taxable supply of goods and/ or services.
- Every registered person is required to **file minimum 25 returns annually.**
- Timely uploading of details of invoices on GSTN in GSTR-1
- Majorly three different types of E-registers will be required to be maintained by taxpayers on GSTN portal. **(7 types of payment forms are there for payment of Tax, Interest and Penalty.)**
- **Late fees of INR 50 per day shall be applicable subject to a maximum of INR 10,000.**

3.2.12 E-way Bill

- E-Way Bill is an electronic document generated on the GST portal evidencing movement of goods.

- **Purpose:** to ensure that goods being transported comply with the GST Law and to track movement of goods and check tax evasion.

- **Who should generate the e-way bill:** the consignor or consignee or the transporter in case the goods are handed over to him and no bill is issued by any above party.

- **When to generate the e-way bill:** As per Rule 138 of the CGST Rules, 2017, every registered person who causes movement of goods (which may not necessarily be on account of supply) of consignment value more than INR 50,000 is required to submit e-way Bill.

- **Cancellation of E-way bill:** if goods are either not transported or are not transported as per the details furnished in the e-way bill, it can be cancelled within 24 hours of generation.

Implementation of E-way Bill System in Different States

- The monetary limit varies from state to state in the range of INR 10,000 to INR 1,00,000.

- In few states, the applicability of e-way bill has been restricted only to inter-city movement having distance more than 50 Km, while few states have mandated e-way bill for intra-city movements without any limit on kilometres.

- Few states have given exemption to certain goods apart from the goods covered in exemption list of Central Government.

- Though the e-way bill is required to be generated mandatorily in case of supply of goods for job work, the state of West Bengal has exempted the transaction of goods sent to job worker and goods sent to another job worker by the job worker.

- On the contrary, Delhi has exempted the generation of e-way bill in case of supply to unregistered person within the state irrespective of value and

distance.

- Further, the states prescribe updated rules for applicability of e-way bill. Hence, the entities having pan-India business need to keep themselves updated with every change in the rules for e-way bill.

- Hence, it can be inferred that the rules of e-way bill are not uniform across the nation and the motto of GST, which is 'One Nation, One tax (law), one market' violates considering the state wise different provisions of e-way bill.

3.2.13 Refunds

- Refund of any tax and interest paid can be claimed by filing of an application before the expiry of 2 years from the relevant date.

- Refund in case of export can be claimed in either of the two options as given below :

  - Refund of unutilized ITC allowed for zero rated supply without payment of tax under LUT / Bond in proportion of export turnover ratio.

  - Refund of GST paid in respect of zero rated supply with payment of tax

- Refund can also be claimed where credit has been accumulated on account of rate of tax on inputs being higher than the rate of taxes on outputs.

3.2.14 TDS Provisions under GST

The provisions of TDS under section 51 have been made applicable with effect from 1 October 2018. Any consideration in excess of INR 2.5 lakhs to be received from following bodies will be subject to TDS @2% (excluding GST and Cess):

- A department or establishment of the Central or State Government (i.e. Department of Pharmaceuticals);

- Local Authority (i.e. Municipal Corporation);
- Governmental Agencies;
- An authority or a board or any other body set up by an Act of Parliament or a State Legislature or established by any Government with 51% or more participation by way of equity or control (i.e. The Central Drugs Standard Control Organization (CDSCO), RBI, IRDA, SEBI, CCI etc.);
- Societies established by CG / SG / LA under the Societies Registration Act, 1860;
- PSUs.

Non Applicability of TDS Provisions

- Provisions of TDS will not be applicable when the location of the supplier and the place of supply is in a State or UT, which is different from the State or UT of registration of the recipient.

Implication of TDS Provisions

- Any contract received from above bodies will attract TDS @2%, which will affect net cash inflow;
- TDS deducted will be reflected in Electronic Cash Ledger, which can be utilised for payment of GST liability or can be claimed as refund from Electronic Cash Ledger.

3.2.15 TCS Provisions under GST

The provisions of TCS have been made applicable with effect from 1 October 2018. Every E-commerce operator is required to collect TCS @1% of the net value of supplies made through such platform.

Implication of TCS provisions:

- Any sale of pharma products through E-commerce platforms will attract TCS @1%, which will affect the net cash flows;
- TCS collected will be reflected in Electronic Cash Ledger, which can be utilised for payment of GST liability or can be claimed as refund from Electronic Cash Ledger.

3.3 Custom Duty

- As per Customs Act, 1962 Custom duty is leviable on exports and imports.
- After GST Implementation, the IGST is levied in replacement of CVD + Special CVD.
- Basic customs duty (BCD) still continues to be levied.
- Import of goods: Taxes leviable = IGST + Education cess + Basic Customs duty + protective taxes such as safe guard duty and anti -dumping (on import of certain goods) +Social welfare surcharge
- Import of services: only IGST will be levied.
- Export of Goods & Services: No GST will be levied. Every exporter files a shipping bill for the goods exported out of India. In this case shipping bill is considered as a deemed application for refund of IGST paid.

Chapter 4

ENTERPRISE RISK MANAGEMENT

Chapter 4 Enterprise Risk Management

4.1 What is Risk?

Risk can be viewed as the combination ofthe probability of an event and the impact of its consequences. Events with a negative impact represent risks that can prevent value creation or erode existing value for its stakeholders. Hence, the organization must understand the types of risks faced by it and address them appropriately.

Generally, risks to the Organization's success can be grouped into four categories: (1) Strategic, (2) Operational, (3) Compliance and (4) Financial & Reporting. Specific examples ofeach type of risk are included in the table below.

Risk Types	Examples
Strategic	– Reduction in business vitality (due to change in business strategy, customer spending patterns, product discovery & development changing technology, etc. Loss of intellectual property & trade secrets) – Competition for talent – Negative impact to reputation/loss of Trustmark
Operational	– Disruption to product supply – Counterfeiting – Inefficient use of resources/increased product cost – Physical property/damage/disruption – Discontinuation of global data flows
Compliance	– Environmental , Employee health & safety – Clinical trial subject/patient safety – Product quality/safety issues(violations of FDA and other Health Authority regulations, Pharma co vigilance) – Selling and promotion of products (including Health Care Compliance (HCC), Foreign Corrupt Practices Act(FCPA)/global Anti-Corruption laws, U.S . government contracts/programs) – Protection of personal deta in accordance with global data protection requirements – Local tax and statutory laws

Risk Types	Examples
Financial & Reporting	– Currency exchange, funding & cash flow, credit risk – Financial statement

- **Key Risk Areas**

The economic and regulatory environment of the pharmaceutical industry has changed and calls for implementation of a sound scientific and risk-based approach towards product development, commercial manufacturing and business operations in general.

This situation demands –

(I) Shorter time-to-market for new medicinal products to make the most out of the available patent-protected time as possible.

(ii) Lean manufacturing processes with quality outcomes to save time and resources for product release.

(iii) Straight communication activities with regulatory authorities too come with delays in market launches and product aviation.

- **Specific Risks to Pharmaceutical Industry include**

a) **Product Liability:** Pharmaceutical companies need to regard product liability as its greatest threat in addition to liability claims which can be covered by traditional risk transfer methods. Companies are more concerned about the damage that a major loss could cause to their image. One of the unique problems in dealing with the product liability is the difficulty of building meaningful risk models. The severity and timing of future claims is highly unpredictable. As a result, the risk managers have to cope with the possibility that a major liability claim can threaten the solvency of their business without their ever knowing just how severe the claim might be.

Although pharmaceutical companies go to great lengths to limit their

product liability risks by using quality assurance techniques, continuous monitoring of product quality and stringent pre–clinical studies and extensive clinical tests that are legally required to be carried out, even the most sophisticated controls cannot entirely prevent the occurrences.

b) **Business Interruption:** The second most critical concern identified is the risk of various breakdowns occurring during production and analytical process. The trend towards centralized production, either in a single unit, or with several units carrying out individual tasks, has increased this risk of product contamination. A single stoppage could have far–reaching consequences.

The effect of business interruption is more complicated in the pharmaceutical industry. To begin with, those who depend on particular medication must continue to receive their supplies. If the pharmaceutical organization has enough inventories to cover the production shortfall, this may not be problematic. Unfortunately, strict regulations governing the storage of drugs combined with their often short shelf–life make this a limited option. Moreover the storage facility itself may have been either lost or contaminated, especially where storage and production occupy nearby units.The risk managers must consider how to replace intermediate compounds and various raw materials including key starting materials used at different stages in the production process and storage of QC rejected finished products under lock and key. The later in the chain the interruption occurs, the harder it is to remedy. To avoid a catastrophic loss, companies must have either the capacity to switch production elsewhere, or be able to produce compounds from other sources.

c) **Patent Infringement:** Protecting intellectual property is considered to be a critical risk for pharmaceutical companies. This reflects the fierce and increasing competitive environment for both R&D and product offerings. The companies need to be generally more concerned about possible financial losses resulting from the infringement of their own patents than about unintentional infringement of other organization's patents.

Moreover, the growing number of counterfeit products hitting the market

represents a considerable threat to the established companies, especially where the copy sports the organization's brand name.

d) **Product Recall:** The risk involved is the subsequent damage to a pharmaceutical business public image. A product image is tarnished by the publicity the product attracts when it is removed from retail shelves. This is aggravated by its unavailability as consumers turn to alternative products. The fundamental goal of a re-launch must be to restore public image.

e) **Research and Development:** The pharmaceutical companies depend increasingly on Research and Development to stay competitive and to promote better earnings growth, especially as profit margins are under increased pressure and market competition has intensified. While events such as fire and natural perils might disrupt or completely destroy an R&D program, wrongly assessed experimental results or new findings in the later stages of product development could prove equally detrimental.

Some risk managers take risk in relation to political risk, foreseeing events – particularly in countries where patent piracy is an issue – that would limit access to essential materials and damage an R&D program.

f) **Environmental Risk:** Environmental risk plays a dominant role in the organization's global risk assessment. The perception of environmental risk is consistent across all corporate types, regardless of whether they have large pharma or chemical or agrochemical units. This growing unease may be rooted in intensified environmental regulations and the host of new laws, or may be due to fears that new risks, such as those related to genetic engineering, will potentially impact the environment.

g) **Other Risks:** Among the multitude of other risks, two merit more detailed consideration: Political risk and financial risk. As far as political risk is concerned, the industry's attention is focused on protecting assets from nationalization, as well as on the potential disturbance of production and distribution. As pharmaceutical companies grow internationally and interdependencies develop, risk managers increasingly have to build global

protection strategies that address the problems associated with political risk.

- **Description of Additional Future key Risks for Pharmaceutical Industry**

  - Intense competition around branded products
  - Costly and highly uncertain nature of R&D
  - Competition from lower-priced generic products
  - Patent loss or expiration in the near future
  - Unexpected development related to safety or efficacy of products
  - Pipeline productivity and competition—ability to continuously develop or replace products
  - Current and future product liability claims
  - Regulatory environment:
    - Potential exposure to government price controls
    - Ability to obtain and maintain approval for products
    - Potential non-compliance issues and scrutiny from regulators
    - Adverse effect from changes in laws and regulations
  - High dependency of revenues, cash flows and earnings on protections given by patents
  - Manufacturing and supply-chain difficulties
  - Reliance on third-party and outsourcing arrangements

4.2 Importance of Quality and Quality Related Risks

Product quality being the main risk for a pharmaceutical industry, the Quality Risk

Management framework becomes an inherent part of an Enterprise Risk Management Framework.

It is particularly useful to have ERM for pharma industry because it faces the complex tasks of developing, testing and manufacturing of drugs, and has rigorous oversight agencies in India and abroad, especially FDA , and serves a marketplace with an exceptionally low tolerance for variability in products.

Yet it is commonly seen that the pharmaceutical industry, like many mature industries, is built around traditional manufacturing processes and legacy information systems. Each is based on rigid work flow patterns that have been optimized for efficiency and cost reductions, rather than for data integration and compliance.

Attaining regulatory compliance within this environment is significant in that the following challenges have to be addressed:

- Isolated work silos exist that have critical information trapped within the manufacturing processes.
- Data redundancies with multiple overlapping reports sometimes confuse and obfuscate further analysis.
- Data communications between processes are missing, and therefore there is no centralized control. Process controls are often localized and do not provide corporate-wide problem remediation.
- Fiscal and operational optimization has a higher priority than the need for compliance.
- Attempts at introducing Enterprise Resource Planning (ERP) systems are often lengthy, time consuming, and expensive and results may only partially address the problem of compliance.

– FDA Initiatives

The FDA uses the concept of risk prevention to focus and drive its initiatives. This leads directly to developing and building verifiable processes that identify, control, and reduce risks in the product or services. In brief, FDA has mandated that the pharmaceutical industry follows the risk methodology outlined below:

- 1st action of an operational risk system is to identify a hazard, non-conformity, or source of variability.
- The next step is to prioritize the seriousness of the risk using FDA and industry standards.
- The system then triggers an alert which serves as a marker for remediation.
- In parallel, the integrated system triggers a system-wide alert and begins the risk log.
- The system then searches for the hazard, as well as the root cause(s) of the problem and corrective mechanisms within the system isolate the threat from the process, and address the root cause(s).

The methodology is iterative, continually searching for and removing remaining residual risks.

These steps provide verifiable oversight and control, without unnecessary complexity.

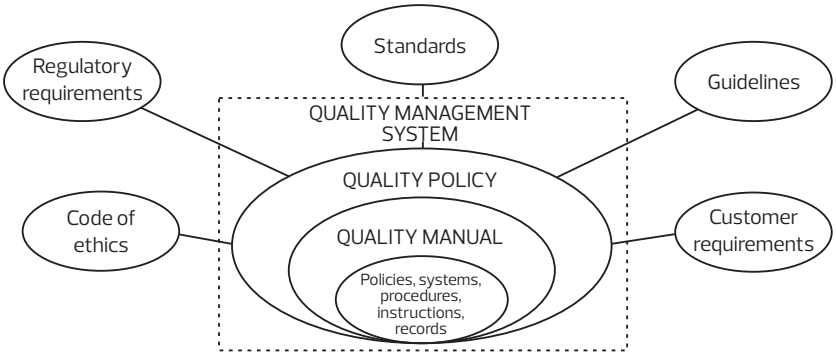
As a minimum, the system continuously monitors key processes, highlighting critical measurement of variability. The FDA then uses the risk methodology to filter and prioritize this data and thereby determine the frequency and severity of a risk for different production practices and design changes.

This is accomplished by applying risk management statistics to the oversight and control systems data. The analysis results in combination with the industries best business practices to provide an on-going evaluation of the severity of each risk against the likelihood of its occurrence. FDA can then compare this information with its industry risk guidelines and its corporate performance history.

- **Quality and the Management of Quality by Quality Risk Management**

Quality planning	Quality improvement	Quality testing/control
Establish quality goals.	Prove the need.	Valuate actual performance.
Identify who the customers are.	Establish the infrastructure.	Act on the difference.
Determine the need of the customers.	Identify the improvement Projects.	Compare actual performance with quality goals.
Developproductfeatures that respond to customers' needs.	Establish project teams.	
Develop processes able to produce product features.	Provide the teams with re-sources, training and motivation to diagnose the causes and stimulate remedies.	
Establish process controls; transfer the plans to the operating forces.	Establish controls to hold the gains.	

– Building Blocks of a Quality Management System



– Resources, Tasks and Related Objects of Pharmaceutical Quality Control

Resources	Tasks	Objects
Adequate facilities	Sampling	Starting materials
Trained personnel	Inspecting	Packaging materials
Approved procedures	Testing	Intermediates
Specifications	Monitoring	Bulk products
Approved RM, KSM, PM	Releasing/rejecting	Finished products
Suppliers	Qualifications	Rejected products
	calibrations	Environmental conditions

– Quality System Elements in the Line of Pharmaceutical Manufacturing as Basis for the Integration of Quality Risk Management

Facilities and equipment	Qualification Equipment Maintenance Equipment Facility cleaning Equipment calibration

Production	Process validation Manufacturing operations Batch record execution and review Product sampling Reprocessing and rework
Packaging and labelling	Packaging operations Packaging materials Receipt, inspection, release and storage Label Reconciliations
Quality control	Sample management Test methods and specifications Method validation Instrument qualification, calibration and maintenance Reference standards management Reagents and solutions management Failure investigation Contract laboratories management
Quality assurance	Documentation management Standard operating procedures, protocols, records, forms, logbooks Training Change control Product quality review(annual product review) Internal and external auditing Complaint management Batch record review and product release Supplier qualification Product stability program Computerized system validation Recalls

4.3 Risk Management

An essential role for business management is to build systems that enhance competitive advantage. While there are different approaches to achieving this, it is fair to say that management seeks on the one had efficiency and effectiveness in its business processes, while on the other hand it looks to minimize and control & other risks. One of the most important features in to risk management is that it evaluates the changing context within the business process model. The FDA and the pharmaceutical industry have an over lapping functionality. Each knows that efficient and effective processes create a strong environment conducive to best business practices.

At each phase of the system life cycle, the FDA and the pharmaceutical industry are on the same page, reviewing the context, identifying and prioritizing the threat level of potential hazardous forces within the environment. It is a shared analysis, looking at the same data, though not necessarily in the same time frame. A pharmaceutical organization would be monitoring and reviewing critical data in real time, and less critical data in a longer time frame. The FDA function is more procedural in that it wants to assure that the pharmaceutical companies have the mechanisms in place to accomplish their tasks in the established timeframe.

Therefore the FDA maintains its oversight of the procedures and evaluative processes, while the pharmaceutical companies focus on building and managing iterative systems that search for those factors which may raise the risk level within the system. These factors include the direct causes of the particular threat, as well as the indirect and secondary causes. Following the identification of the hazard, there is a determination of its probability of occurrence as well as the potential damage. This is standard decision making theory where risk is the probability of occurrence of loss multiplied by its respective magnitude. Risk management then uses FDA approved best business practices to establish procedures for preventive or corrective actions. This approach is particularly valuable in an environment where multiple, seemingly negligible risks have the combined potential to cause harm.

4.3.1 Risk Modeling In Pharmaceutical Manufacturing

The stated goals of the pharmaceutical industry are to manufacture products with the highest quality, safety and efficacy, at the lowest responsible cost. In order to achieve these goals the industry has to focus on process design in manufacturing, supply chain management, and overall system security. Overtime, hazards and variability have been reduced, and manufactured products have achieved a very safe tolerance level. Much of this has been accomplished using traditional design methodologies that focus on building systems that meet fixed specifications. These improvements come from best practices and regulatory guidelines that address problems with quality, variability in processes, time induced degradations, and the like.

Risk methodology provides additional tools to accomplish these objectives. In fact BPM and best practices are strengthened by the formal acknowledgement of risk and procedures for CAPA mitigation. These can act as an overall catalyst for the elimination of system stoppages and failures on one hand and on the other are the basis for cost effective management and production. In this way managers can guarantee system and product integrity, and provide compliance in real time reports. This is the needed assurance that companies are meeting both their internal objectives as well as the necessary regulatory inspection standards for pharmaceutical products.

4.3.2 Key Aspects of a Sound Risk Management Strategy in the Pharmaceutical Industry

(a) Stepwise, companywide integration of risk-based approaches, starting with the quality systems and gradually expanding risk management with regard to other relevant systems and development of an adequate risk culture.

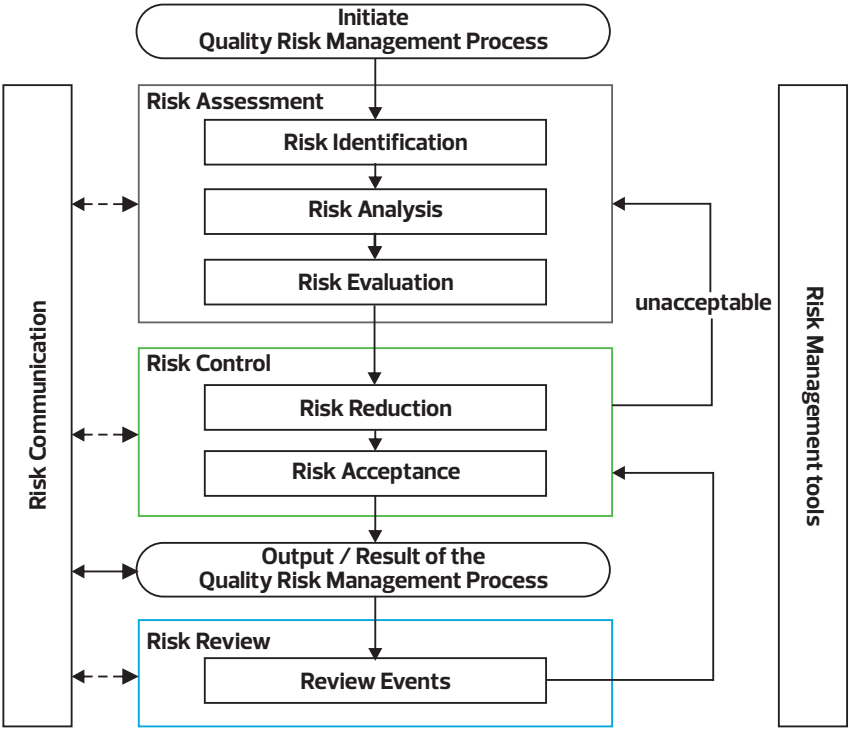
(b) Constantly review and improve the already existing risk management system with regards to costs, overall business strategy and regulatory demands.

The pharmaceutical industry is a high-tech industry with high value-added products. Generally pharmaceutical plants manufacture two different types of products, over-the-counter and prescription products.

Risks could be involved in the following stages:

- Typically, in the manufacturing process, various chemicals are handled through several equipment, machinery and processes using electricity and mechanical devices. Various microorganisms are also handled both in the laboratory and in production process.
- It is necessary to thoroughly study the whole setup, machinery, process, raw materials, chemicals, microorganisms, and also identify all possible hazards and then take preventive and corrective measures to prevent the possibility of accidents.
- Thus, it is necessary to consider all the above aspects for safety purpose during planning and implementation of project. This helps in prevention of accidents during running of plant.
- Hazards in this industry include fire or explosion through solvents, flammable liquids or dusts and the resulting contamination of production and storage areas, particularly clean rooms by smoke or other substances released by the fire or equipment damage.
- Due to the medical nature of the products produced, companies may only be licensed to manufacture at specific production facilities. Re-certification of contaminated production lines can be a lengthy procedure and can lead to a loss of market share.

4.3.3 Risk Management Process



4.3.4 Process Management Repository

A process management repository would contain data and methods which under pin best practices, risk management and compliance with the FDA.

The Enterprise Risk Management (ERM) frame work described by the Committee of Sponsoring Organizations of the Tread way Commission (COSO) and those of IT Governance Institute's (ITGI) COBIT4.0 methodology partially outline this approach.

With the ERM framework, companies can build a broad enterprise-wide system of internal controls and management practices. The ITGI's framework is also broad but more focused on developing a roadmap for IT best practices. In fact part of the ITGI best practices comes from the (ERM) framework. The overall result is that

both the ERM and COBIT frameworks address building an overall philosophy, as well as infrastructure to manage both risk and performance.

These functional aspects of ERM and COBIT can be implemented using knowledge management systems, and in particular its process management repository (PMR). This implementation would use such tools as data dictionaries describing risk classes, repositories for storing critical compliance information, best practices, CAPA methods/procedures, and performance measurements using the same logic, a PMR could very well be the basis for a future FDA infrastructure focusing on the immediate need for oversight and the reduction of risk. This infrastructure would actively manage best practice and verifiable compliance. Therefore a critical element in moving to the FDA model, or to any risk centered model, is the successful conceptualizing and implementation of a process repository.

Some of the characteristics of the repository for the pharmaceutical industry could be:

- FDA regulations
- Corporate policies and procedures
- Corporate environment for risk management with supporting surveys
- Industry best practice mandates with supporting evidence
- Test plans with test outcomes
- Business process flows, theoretical and actual
- Risk libraries with stored CAPA plans and self-activated procedures
- Control libraries documenting control history
- Evidence for compliance in a transparent electronic format

This is spelled out in greater detail in the table on the next page. The process repository outlined in this table becomes part of the overall knowledge

management system that meets the compliance mandate of the FDA. Its functionality permits on one hand the codifying and storing of best practices and critical data. On the other hand it provides active management of risk accounting and fault management. It is direct and focused for FDA oversight, and provides the foundation for further steps as the FDA matures and adopts specifications similar to ERM and COBIT.

4.3.5 Process Repository

Repository Management	Risk Component
Regulatory database	Data repository of regulatory standards and critical measurements
Best Practice database	Industry standard procedures
Compensatory Services	CAPA programs and procedures with triggers
Accounting Management	
Mapping of processes	Detailed description of processes and risks
Logistic tracking	Tracking of resources, products, processes
Data comparison	Analysis of critical measurements and variability
Change tracking	Monitoring change in the process
Design optimization	Planning for performance upgrades
Audit	Audit trail showing data creation, modification, deletion
Plug and play configuration	Incorporating new systems
Fault Management	
Alarm notification	Alerting staff and control hardware of faults
Alarm correction	Switching, and isolating supplies, processes and Products
Disaster recovery	Isolating and recovering from disasters; logging activities, switching over to redundant systems
Remote process Reconfiguration	Modifying process using CAPA
Performance Management	
Capacity planning	Tracking production growth

Repository Management	Risk Component
Event scheduling	Balancing production loads of scheduled processes
Process analysis	Analysing for errors and faults, using best practices
Test monitoring	Testing samples for quality and performance
Trouble ticketing	Resolving known problems and replacing defects
Information Management	
Data backup	Securing data and configuration information
Monitoring and testing control Mechanisms	Checking system controls with test data
Creating transparency for internal usage and for Regulatory Agency	Shared protocols for transferring information internally and externally
Developing dashboards to quantify risks	Straightforward visual metering of risk and performance Levels
Firewall filtering services	Screening the information repository and monitoring against foreign activity

4.4 Benefits of an Effective Risk Management Framework

ERM is a common framework applied by business management and other personnel to identify potential events that may affect the enterprise managing the associated risks and opportunities and provide reasonable assurance that organization's objectives are achieved.

Through this approach to risk management, it can:

- Ensure prompt resolution of internally identified risks in compliance with laws and regulations to maintain the provision of quality products, protect patient safety and ensure appropriate relationships with customers.
- Support "simplification" strategies to ensure effective use of resources, enable an optimized approach to auditing and identification/remediation of compliance issues and promote reporting and monitoring across compliance functions.

- Enable improved decision making, planning and prioritization through a structured understanding of opportunities and threats.

- Support value creation by enabling management to deal effectively with future events that create uncertainty, pose a significant risk or opportunity and to respond in a prompt, efficient and effective manner.

- Support growth drivers of creating value through innovation, extending our global reach with local focus, executing with excellence and leading with purpose.

4.4.1 Risk Review

The output/results of the risk management process should be reviewed to take into account new knowledge and experience. A quality risk management process should continue to be utilized for events that might impact the original quality risk.

These events can be planned or unplanned. E.g.

Sr.No.	Planned events	Unplanned Events
1.	Results of product review	Break down during manufacturing process i.e Equipment/instrument breakdown
2.	Outcome of inspections and audits	Root cause from failure investigation
3.	Change controls	Product recall
4.	Planned deviation	Unplanned deviations
5.	Outcome of cost effective changes	Market complaint

Risk review might include reconsideration of risk acceptance decisions.

Risk review should be an on-going part of the quality management process, a mechanism to review or monitor such events should be implemented.

4.4.2 Risk Management Methods and Tools

Sr.No.	Risk Management Methods and Tools	Potential Areas of Use
1.	Failure Mode Effects Analysis (FMEA)	– It can be applied to equipment and facilities and might be used to analyze a manufacturing operation and its effect on product or process. – It identifies elements/operations within the system.
2.	Failure Mode, Effects and Criticality Analysis (FMECA)	– It can be utilized for failures and risks associated with manufacturing processes; however, it is not limited to this application.
3.	Fault Tree Analysis (FTA)	– It can be used to establish the pathway to the root cause of the failure. – FTA can be used to investigate complaints or deviations.
4.	Hazard Analysis and Critical Control Points (HACCP)	– It might be used to identify and manage risks associated with physical, chemical and biological hazards (including microbiological contamination).
5.	Hazard Operability Analysis (HAZOP)	– HAZOP can be applied to manufacturing processes, including outsourced production and formulation. – It can be used for upstream suppliers, equipment and facilities for drug substances and drug (medicinal) products.
6.	Preliminary Hazard Analysis (PHA)	– PHA might be useful when analyzing existing systems or prioritizing hazards where circumstances prevent a more extensive technique from being used. – It can be used for product, process and facility design as well as to evaluate the types of hazards for the general product type and product class.

Sr.No.	Risk Management Methods and Tools	Potential Areas of Use
7.	Risk Ranking and Filtering	– It can be used to prioritize manufacturing sites for inspection/audit by regulators or industry. – It is used to evaluate both quantitatively-assessed and qualitatively-assessed risks within the same organizational framework.
8.	Supporting Statistical Tools	– To identify potential uses of quality risk management principles and tools by industry and regulators.

Chapter 5

COMPLIANCES REQUIRED FROM AN INDIAN PHARMACEUTICAL COMPANY

Chapter 5 Compliances Required from an Indian Pharmaceutical Company

In this chapter we have enumerated certain governing bodies who oversee the compliances of Indian pharmaceutical industry.

5.1 Indian Regulations and Guidelines

5.1.1 Central Drugs Standard Control Organization (CDSCO)

- In India, CDSCO is the national regulatory body for Indian pharmaceuticals and medical devices, serves parallel function to the European Medicines Agency of the European Union, the PMDA of Japan, the Food and Drug Administration of the United States and the Medicines and Healthcare products Regulatory Agency of the United Kingdom.
- Functions undertaken by the Central authority and state authorities can be summarized as:

Central Authority	State Authorities
Lay down standards of drugs, cosmetics, diagnostics and devices.	Licensing of drug manufacturing and sales establishments.
Lay down regulatory measures, amendments to Acts and Rules.	Licensing of drug testing laboratories.
Regulate market authorization of new drugs.	Approval of drug formulations for manufacture.
Approve licenses to manufacture certain categories of drugs as Central Licence approving Authority i.e. for Blood Banks, Large Volume Parenteral and Vaccines & Sera.	Monitoring of quality of Drugs & Cosmetics, manufactured by respective state units and those marketed in the state.
Work relating to the Drugs Technical Advisory Board (DTAB) and Drugs Consultative Committee (DCC).	Investigation and prosecution in respect of contravention of legal provisions.
Regulate the standards of imported drugs.	Administrative actions.
Testing of drugs by Central Drugs Labs.	Pre- and post- licensing inspection.
Publication of Indian Pharmacopoeia.	Recall of sub-standard drugs.

- **Requirements for approval of clinical trials and new drugs**

General Requirements	Documents Requirement
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.	– Cover in Letter – Authorization Letter – Form 40 – TR6 Challan (Fees) – Power of Attorney – Wholesale License – Schedule D(I) – Schedule D(II) – Free Sale Certificate – GMP Certificate of WHO guideline or Certificate of Pharmaceutical Product (COPP) – Manufacturing License and /or Market authorization Certificate – Establishment License – Inspection/Audit Report – Re– registration undertaking
Entirely original data, data from the literature, both original data and data from the literature ("hybrid").	
Chemical and pharmaceutical data should always be original, unless there is sufficient justification with literature in case partial data is not original.	
The office of DCG (I) grants approval of manufacture / import of new drugs for marketing in the country.	
No clinical trial for a new drug, whether for clinical investigation or any clinical experiment by any institution, shall be conducted except under, and in accordance with, the permission, in writing, of the Licensing Authority defined in clause (b) of Rule 21.	

5.1.2 NPPA Drugs (Price Control) Order 1995 and other orders enforced by National Pharmaceutical Pricing Authority (NPPA), Government of India.

- **Applicability of the Law**

Commonly used bulk drugs are kept under statutory price control. All formulations containing these bulk drugs either in a single or combination form fall under price controlled category. However, the prices of other drugs can be regulated, if warranted in public interest.

– **Procedure for calculating ceiling price**

(1) The ceiling price of a scheduled formulation of specified strengths and dosages as specified under the first schedule shall be calculated as under:

Step 1: Average Price to Retailer, P(s)

$$P(s) = \frac{\text{Sum of prices to retailer of all the brands and generic versions of the medicine having market share more than or equal to 1\% of the total market turnover on the basis of moving annual turnover of that medicine.}}{\text{Total number of such brands and generic versions of the medicine having market share more than or equal to 1 \% of total market turnover on the basis of moving annual turnover for that medicine.}}$$

Step 2: Thereafter, the ceiling price of the scheduled formulation i.e.

P(c) shall be calculated as below:

$P(c) = P(s) \times (1+M/100)$

Where

P(s) = Average Price to Retailer for the same strength and dosage of the medicine as calculated in step 1 above.

M = % Margin to retailer and its value = 16

(2) The ceiling price calculated as per sub –paragraph (1) and notified by the Government shall be applicable to scheduled imported formulations also.

5.1.3 The Drugs & Cosmetics Act, 1940: The Drugs and Cosmetics Act, 1940 regulates the import, manufacture and distribution of drugs in India. The primary objective of

the Act is to ensure that the drugs and cosmetics sold in India are safe, effective and conform to state quality standards. It contains 168 rules and 25 schedules.

Sr.No	Schedule	Title
1.	Schedule A	Various forms and formats of letters for applications of licensing etc.
2.	Schedule B	Fees structure for government-run labs.
3.	Schedule C	Various biological products regulation. E.g. Serums, Adrenalines.
4.	Schedule D	List of drugs exempted from the provision of import of drugs
5.	Schedule E	Various poisons and their regulation. Examples: Sarpa Visha (Snake venom), Parada (Mercury) etc.
6.	Schedule F	Regulations and standards for running a blood bank
	Schedule F-I	Regulations and standards for vaccines
	Schedule F-II	Contains regulations and standards for surgical dressing.
	Schedule F-III	Regulations and standards for umbilical tapes
7.	Schedule F-F	Regulations and standards for ophthalmic ointments and solutions.
8.	Schedule G	Hormonal preparations.
9.	Schedule H	Prescription Drugs
10.	Schedule I	Omitted
11.	Schedule J	List of various diseases and conditions that cannot be treated under any drug currently in market. No drug may legally claim to treat these diseases.
12.	Schedule K	Contains class of drugs: Extent and condition of exemption
13.	Schedule L1	Good Laboratory Practice
14.	Schedule M	Good Manufacturing practice
15.	Schedule N	Regulations and requirements for a pharmacy.
16.	Schedule O	Various regulations and requirements for disinfectant fluids.
17.	Schedule P	Regulations regarding life period and storage of various drugs.

Sr.No	Schedule	Title
18.	Schedule Q	List of permitted dyes and pigments in soap and cosmetics.
19.	Schedule R	Requirements for condoms and other mechanical contraceptives
20.	Schedule S	Standards for cosmetics
21.	Schedule T	Good manufacturing procedure for Ayurvedic, Siddha and Unani products
22.	Schedule U Schedule UI Schedule UII Schedule UIII	Regulations and requirements for record keeping Manufacturing records Raw materials records Analytical records
23.	Schedule V	Standards for drug patents
24.	Schedule W	Omitted
25.	Schedule X	Regulations and guidelines on Narcotic drugs
26.	Schedule Y	Requirement and guidelines for clinical trials

The related Drugs and Cosmetics Rules, 1945 contain provisions for classification of drugs under given schedules and there are guidelines for the storage, sale, display and prescription of drugs mentioned in each schedule.

Labels on packages or containers of drugs for export shall be adapted to meet the specific requirements of the law of the country to which the drug is to be exported but the following particulars shall appear in a conspicuous position on the innermost container in which the drug is packed and every other covering in which that container is packed:

(a) Name of the drug;

(b) Name, address of the manufacturer and the number of the licence under which the drug has been manufactured;

(c) Batch or lot number;

(d) Date of expiry.

- Following bodies have been defined under the Act:

The Drugs Technical Advisory Board	The Central Drugs Laboratory	The Drugs Consultative Committee
To advise the Central Government and the State Governments on technical matters arising out of the administration of this Act and to carry out the other functions assigned to it by this Act.	To carry out the functions entrusted to it by this Act or any rules made under this Chapter.	To advise the Central Government, the State Governments and the Drugs Technical Advisory Board on any other matter tending to secure uniformity throughoutIndia in the administration of this Act.

- The Act also specifies misbranded, adulterated and spurious drugs (i.e. those drugs and cosmetics which do not comply with the prescribed quality standards) as below:

Terms	Definition
Misbranded	– Coloured, coated, powdered or polished such that the damage is concealed or if it is made to appear of better or greater therapeutic value than it really is. – Not labelled in the prescribed manner. – If its label or container or anything accompanying the drug bears any statement, design or device which makes any false claim.
Adulterated	– If it consists in whole or in part, of any filthy, putrid or decomposed substance. – If it has been prepared, packed or stored under insanitary conditions whereby it may have been contaminated. – If itscontainer is composed in whole or in part, of any poisonous or deleterious substance. – If it contain a colour other than one which is prescribed.
Spurious	– Manufactured under a name which belongs to another drug. – If the label or container bears the name of an individual or organization purporting to be the manufacturer of the

Terms	Definition
	drug, which is fictitious or does not exist. – If it purports to be the product of a manufacturer of whom it is not truly a product.

– **Prohibitions**

Import of Certain Drugs or Cosmetics	Manufacture & Sale of Certain Drugs and Cosmetics
Substandard, Misbranded, spurious, adulterated.	Substandard, Misbranded, spurious, adulterated.
Any drug or cosmetic the import of which is prohibited by rule.	Manufactured with contravention of any of the provisions of this Chapter or any rule made there under.
Not licensed or not mentioned in license.	
Any patent or proprietary medicine, unless there is display in the prescribed manner on the label or container.	
Any cosmetic containing any ingredient which may render it unsafe or harmful for use under the directions indicated or recommended.	

– **Maintenance of records and furnishing of information:**

Every person holding a licence under clause (c) of section 33EEC shall keep and maintain such records, registers and other documents as may be prescribed and shall furnish to any officer or authority exercising any power or discharging any function under this Act such information as is required by such officer or authority for carrying out the purposes of this Act.

5.1.4 GCP Guidelines: The Ministry of Health, along with **Drugs Controller General of India (DCGI) and Indian Council for Medical Research (ICMR)** has come out with draft guidelines for research in human subjects. These GCP guidelines are essentially based on Declaration of Helsinki, WHO guidelines and ICH requirements for good clinical practice.

5.1.5 The Pharmacy Act, 1948: The Pharmacy Act, 1948 is meant to regulate the

profession of pharmacy. This Act regulates:

- Registration of pharmacists.
- Qualifications for subsequent registration.
- Removal of name of registered pharmacists from register.
- Penalty for falsely claiming to be registered.

5.1.6 The Drugs and Magic Remedies (Objectionable Advertisement) Act, 1954:

Provides to control the advertisements regarding drugs and advertising of remedies alleged to possess magic qualities.

5.1.7 The Narcotic Drugs and Psychotropic Substances Act, 1985:

An act concerned with control and regulation of operations relating to Narcotic Drugs and Psychotropic Substances.

- **Prohibition of certain operations**

  No person shall

  a) Cultivate any coca plant or gather any portion of coca plant; or

  b) Cultivate the opium poppy or any cannabis plant; or

  c) Produce, manufacture, possess, sell, purchase, transport, warehouse, use, consume, import inter-State export inter-State import into India, export from India or tranship any narcotic drug or psychotropic substance, except for medical or scientific under authorization.

- **Prohibition of certain activities relating to property derived from offence**

  No person shall convert or transfer any property knowing that such property is derived from an offence committed under this Act or under any other corresponding law of any other country or from an act of participation in such offence, for the purpose of concealing or disguising the

illicit origin of the property or to assist any person in the commission of an offence or to evade the legal consequences.

- **Restrictions over external dealings in narcotic drugs and psychotropic substances**

  No person shall engage in or control any trade whereby a narcotic drug or psychotropic substance is obtained outside India and supplied to any person outside India save with the previous authorisation of the Central Government and subject to such conditions as may be imposed by that Government in this behalf.

- **Special provisions relating to coca plant and coca leaves for use in the preparation of flavouring agent**

  The Central Government may permit, with or without conditions, and on behalf of Government, the cultivation of any coca plant or gathering of any portion thereof or the production, possession, sale, purchase, transport, import inter-State, export inter-State or import into India of coca leaves for use in the preparation of any flavouring agent which shall not contain any alkaloid and to the extent necessary for such use.

- **Special provision relating to cannabis**

  Government may permit, by general or special order and subject to such conditions as may be specified in such order, cultivation of any cannabis plant for industrial purposes only of obtaining fibre or seed or for horticultural purposes.

- **Penalty**

  Whoever contravenes any provisions of this Act or any rule or order made or condition of licence granted thereunder shall be punishable with fine and rigorous imprisonment as per the laws drafted thereunder according to the nature of offence.

5.2 International Regulations and Guidelines and Certain Regulatory Bodies

- **World Health Organisation (WHO) guidelines** oversee the medicines policy, intellectual property rights, financing & supply management, quality & safety, selection & rational use of medicines, technical co-operation and traditional medicines.
- **International Council on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH)** guidelines define quality, safety, efficacy and related aspects for developing and registering new medicinal products in Europe, Japan and the United States.
- **Organization for Economic Collaboration and Development:** This organisation, with 30 member countries regulate the economic and social issues in areas of health care.
- **European Medicines Agency (EMEA):** Decentralized body of the European Union headquartered in London, prescribes guidelines for inspections and general reporting and all aspects of human and veterinary medicines in the European Union.
- Regulations, guidelines, notifications, news and communications from **US Food and Drug Administration.**
- Specifications regulating medicines, medical devices, blood, tissues and chemicals, issued by **Therapeutic Goods Administration**, the Australian regulatory body.
- **The Department of Health, South Africa.**
- News, resources, documents and publications of the **World Trade Organization (WTO),** the global international organization dealing with the rules of trade between nations.
- Collection of international food standards and guidelines for processed, semi—processed and raw foods, adopted by the **Codex Alimentarius**

Commission under the Joint FAO / WHO Food Standards Programme.

- News, warnings, information and publications of **Medicines and Healthcare products Regulatory Agency (MHRA)**, responsible for ensuring efficacy and safety of medicines and medical devices in the **UK.**
- Advisories, warnings, recalls, reports, publications, activities, legislations and guidelines from **Health Canada**, the Federal Department responsible for health related issues in Canada.
- **Thai Food and Drug Administration** laws and regulations with respect to drugs, food, cosmetics and narcotics.
- **Health Sciences Authority (HSA), the regulatory body of Singapore.**
- **The Department of Health, Philippines.**
- **Medsafe,** New Zealand Medicines and Medical Devices Safety Authority.
- Regulatory information, news and publications of **National Pharmaceutical Control Bureau, Malaysia.**
- Guidelines and useful information to ensure safety, efficacy and quality of medicines, issued by **Directorate-General Medicinal Products, Belgium.**
- Licensing and registration guidelines for medicinal products laid down by **Federal Institute for Drugs and Medical Devices, Germany.**
- **Swiss regulatory agency** for therapeutic products.
- Regulatory and surveillance guidelines issued by **Medical Products Agency, Sweden.**
- News, regulations and guidelines issued by **The National Agency for Food Administration and Control (NAFDAC), Nigeria.**
- **The national health surveillance agency (ANVISA, Brazil).**

Chapter 6

GOOD MANUFACTURING PRACTICE

Chapter 6 Good Manufacturing Practice (Schedule M to Drugs and Cosmetics Act, 1940)

6.1 Good Manufacturing Practices (GMP) for Premises And Materials

Schedule M to the Drugs and Cosmetics Act, 1940 prescribes certain GMP and mandatory requirements in respect of maintaining premises, plant and equipment for pharmaceutical products. We have covered in brief certain important provisions of the schedule.

6.1.1 General Requirements

- **Location and surroundings:** The factory building(s) for manufacture of drugs shall be so situated and shall have such measures as to avoid risk of contamination from external environmental including open sewage, drain, public lavatory or any factory which product disagreeable or obnoxious odour, fumes, excessive soot, dust, smoke, chemical or biological emissions.

- **Building and premises:** The building(s) used for the factory shall be designed, constructed, adapted and maintained to suit the manufacturing operations so as to permit production of drugs under hygienic conditions which shall be compatible with other drug manufactured in same or adjacent area, adequately provided with working space to avoid cross contamination and contamination of foreign particles. They shall conform to the conditions laid down in the Factories Act, 1948.

- **Water system:** Water system should be in accordance with the standards specified by the Bureau of Indian Standards or Local Municipality, so as to produce and store purified water conforming to pharmacopoeial specification. The storage tank shall be cleaned periodically and records maintained by the licensee in this behalf.

- **Disposal of waste**: The disposal and storage of sewage, effluents (solid, liquid, gas, bio medical waste, hazardous, toxic substances and flammable materials) and rejected drugs from the manufactory shall be in conformity with the requirements of Environment Pollution Control Board.

6.1.2 Warehousing Area

- Adequate areas shall be designed to allow sufficient and orderly warehousing of various categories of materials and products like starting and packaging materials, intermediates, bulk and finished products, products in quarantine, released, rejected, returned or recalled, machine and equipment spare parts, highly hazardous, poisonous and explosive materials, narcotics, psychotropic drugs and substances presenting potential risks of abuse, fire or explosion and change items.

- Warehousing areas shall be designed and adapted to ensure good storage conditions. They shall be clean, dry and maintained with acceptable temperature limits, where special storage conditions are required (e.g. temperature, humidity), these shall be provided, monitored and recorded.

6.1.3 Production Area

- Design of the production area should ensure the carrying out of production process process in uni–flow and with logical sequence of operations to avoid the risk of cross–contamination, separate dedicated and self–contained facilities shall be made available for the production of sensitive pharmaceuticals (penicillin or biological preparations).

- Pipe–work, electrical fittings, ventilation openings and similar services lines shall be designed, fixed and constructed to avoid creation of recesses.

6.1.4 Ancillary Areas

- Rest and refreshment rooms shall be separate from manufacturing and storage areas.

- Maintenance workshops shall be separate and away from production areas. Whenever spares, changed parts and tools are stored in the production area, these shall be kept in dedicated rooms or lockers. Tools and spare parts for use in sterile areas shall be disinfected before these are carried inside the production areas.

- Area housing animals shall be isolated from other areas. The other requirements regarding animal houses shall be those as prescribed in Rule 50-C(3) of the Drugs and Cosmetics Rules, 1945 which shall be adopted for production purposes.

6.1.5 Quality Control Area

- Quality Control Laboratories shall be independent of the production areas. Separate areas shall be provided each for physico-chemical, biological, microbiological or radio-isotope analysis. Separate instrument room with adequate area shall be provided for sensitive and sophisticated instruments employed for analysis.

- The design of the laboratory shall take into account the suitability of construction materials and ventilation. Separate air handling units and other requirements shall be provided for biological, microbiological and radioisotopes testing areas.

- The microbiology section shall have arrangements such as airlocks and laminar air flow work station, wherever considered necessary.

6.1.6 Personnel

- The manufacture, quality control and quality assurance activities shall be conducted under the direct supervision of competent technical staff with prescribed qualifications and practical experience in the relevant dosage and / or active pharmaceutical products.

- Written duties of technical and quality control personnel shall be laid down and followed strictly.

- The licencee (by way of written instruction) should ensure that all the personnel in production area / quality control laboratories are periodically trained appropriately considering their duties and responsibilities.

6.1.7 Health, Clothing and Sanitation of Workers

- The personnel handling Beta-lactam antibiotics shall be tested for Penicillin sensitivity before employment and those handling sex hormones, cytotoxic substances and other potent drugs shall be periodically examined for adverse effects. These personnel should be moved out of these sections (except in dedicated facilities), by rotation, as a health safeguard.

- Pre-employment medical examination in respect of certain prescribed diseases and regular examinations of the existing personnel (atleast once in a year) including documentation thereof is mandatory. The licensee shall provide the services of a qualified physician for assessing the health status of personnel involved in different activities.

- No person showing, at any time, apparent illness or open lesions which may adversely affect the quality of products, shall be allowed to handle starting materials, packing materials, in-process materials, and drug products until his condition is no longer judged to be a risk.

- All personnel shall be instructed to report about their illness or abnormal health condition to their immediate supervisor so that appropriate action can be taken.

- All personnel shall wear clean body coverings appropriate to their duties.

- Smoking, eating, drinking, chewing or keeping plants, food, drink and personal medicines shall not be permitted in production, laboratory, storage and other areas where they might adversely influence the product quality.

6.1.8 Manufacturing Operations and Controls

- All manufacturing operations shall be carried out by trained personnel under the supervision of technical staff approved by the Licensing Authority.

- The contents of all vessels and containers used in manufacture and storage during the various manufacturing stages shall be conspicuously labelled

with the name of the product, batch number, batch size and stage of manufacture. Each label should be initialled and dated by the authorised technical staff. Products not prepared under aseptic conditions are required to be free from pathogens like Salmonella, Escherichia coli, Pyocyanea, etc.

Precautions against mix–up and cross–contamination

- To prevent mix–ups during production stages, materials under process shall be conspicuously labelled to demonstrate their status. All equipment used for production shall be labelled with their current status.
- Packaging lines shall be independent and adequately segregated. It shall be ensured that all left–overs of the previous packaging operations, including labels, cartons and caps are cleared before the closing hour.
- Before packaging operations are begun, steps shall be taken to ensure that the work area, packaging lines, printing machines, and other equipment are clean and free from any products, materials and spillages. The line clearance shall be performed according to an approximate check–list and recorded.
- The correct details of any printing (for example of batch numbers or expiry dates) done separately or in the course of the packaging shall be rechecked at regular intervals. All printing and overprinting shall be authorized in writing.
- The manufacturing environment shall be maintained at the required levels of temperature, humidity and cleanliness.
- Authorised persons shall ensure change–over into specific uniforms before undertaking any manufacturing operations including packaging.
- There shall be segregated enclosed areas, secured for recalled or rejected material and for such materials which are to be reprocessed or recovered.

6.1.9 Sanitation in the Manufacturing Premises

- The manufacturing premises shall be cleaned and maintained in an orderly

manner, so that it is free from accumulated waste, dust, debris and other similar material. A validated cleaning procedure shall be maintained.

- The manufacturing areas shall not be used for storage of materials, except for the material being processed. It shall not be used as a general thoroughfare.

- A routine sanitation program shall be drawn up and observed, which shall be properly recorded and which shall indicate—

  (a) Specific areas to be cleaned at cleaning intervals;

  (b) Cleaning procedure to be followed, including equipment and materials to be used for cleaning;

  (c) Personnel assigned to and responsible for the cleaning operation.

- Production areas shall be well lit, particularly where visual on-line controls are carried out.

6.1.10 Raw Materials

- The licensee shall keep an inventory of all raw materials to be used at any stage of manufacture of drugs and maintain records as per **"Schedule U" of Drug and Cosmetic Act 1940.**

- All incoming materials shall be quarantined immediately after receipt or processing. All materials shall be stored under appropriate conditions and in an orderly fashion to permit batch segregation and stock rotation by a first in/first expiry or first-out principle.

- All incoming materials shall be purchased from approved sources under valid purchase vouchers. Wherever possible, raw materials should be purchased directly from the producers.

- Authorized staff appointed by the licensee in this behalf, which may include personnel from the Quality Control Department, shall examine each

consignment on receipt and shall check each container for integrity of package and seal. Damaged containers shall be identified, recorded and segregated.

- If a single delivery of material is made up of different batches, each batch shall be considered as a separate batch for sampling, testing and release.
- Raw materials in the storage area shall be appropriately labelled. Labels shall be clearly marked with the following information:

  (a) Designated name of the product and the internal code reference, where applicable, and analytical reference number;

  (b) Manufacturers name, address and batch number manufacturing date, expiry date and re-test date;

  (c) The status of the contents (e.g. quarantine, under test, released, approved, rejected);

- There shall be adequate separate areas for materials under test, approved and rejected with arrangements and equipment to allow dry, clean and orderly placement of stored materials and products, wherever necessary, under controlled temperature and humidity.
- Containers from which samples have been drawn shall be identified.
- Only raw materials which have been released by the Quality Control Department and which are within their shelf-life shall be used. It shall be ensured that shelf life of formulation product shall not exceed with that of active raw materials used.
- It shall be ensured that all the containers of raw materials are placed on the raised platforms/racks and not placed directly on the floor.

6.1.11 Equipment

- Equipment shall be located, designed, constructed, adapted and maintained

to suit the operations to be carried out. The layout and design of the equipment shall aim to minimise the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build-up of dust or dirt and, in general any adverse effect on the quality of products. Each equipment shall be provided with a logbook, wherever necessary.

- Balances and other measuring equipment of an appropriate range, accuracy and precision shall be available in the raw material stores, production and in process control operations and these shall be calibrated and checked on a scheduled basis in accordance with standard operating procedures and records maintained.

- The parts of the production equipment that come into contact with the product shall be inert

- To avoid accidental contamination, wherever possible, non-toxic/edible grade lubricants shall be used and the equipment shall be maintained in a way that lubricants do not contaminate the products being produced.

6.1.12 Documentation and Records

- Documentation plays a crucial role for any quality assurance system. It defines the standard operating procedures and also provides audit trail and investigation in case of any suspicious transactions for various activities undertaken. Documents designed, prepared, reviewed, approved and controlled by authorized persons wherever applicable, shall comply with these rules.

- Documents shall specify the title, nature and purpose. and shall be laid out in an orderly fashion and be easy to check. Reproduced documents shall be clear and legible. Documents shall be regularly reviewed and kept up to date. Any alteration made in the entry of a document shall be signed and dated.

- The records shall be made or completed at the time of each operation in such a way that all significant activities concerning the manufacture of

pharmaceutical products are traceable. Records and associated Standard Operating Procedures (SOP) shall be retained for at least one year after the expiry date of the finished product.

- Data may be recorded by electronic data processing systems or other reliable means, but Master Formulae and detailed operating procedures relating to the system in use shall also be available in a hard copy to facilitate checking of the accuracy of the records. Wherever documentation is handled by electronic data processing methods, authorized persons shall enter modify data in the computer. There shall be record of changed and deletions. Access shall be restricted by passwords or other means and the result of entry of critical data shall be independently checked. Batch records electronically stored shall be protected by a suitable back–up. During the period of retention, all relevant data shall be readily available.

6.1.13 Labels and Other Printed Materials

Labels are absolutely necessary for identification of the drugs and their use. The Printing shall be done in bright colours and in a legible manner. The label shall carry all the prescribed details about the product.

- All containers and equipment shall bear appropriate labels. Different colour coded tablets shall be used to indicate the status of a product (for example under test, approved, passed, rejected).

- To avoid chance mix–up of printed packaging materials, product leaflets, relating to different products, shall be stored separately.

- Prior to release, all labels for containers, cartons and boxes and all circulars, inserts and leaflets shall be examined by the Quality Control department of the licensee.

- Prior to packaging and labelling of a given batch of a drug, it shall be ensured by the licensee that samples are drawn from the bulk and duly tested, approved and released by the quality control personnel.

5. Records of label reconciliation shall be maintained.

6.1.14 Quality Assurance

Quality assurance is the totality of the arrangements made with the object of ensuring that products are of the quality required for their intended use.

The system of quality assurance appropriate to the manufacture of pharmaceutical products shall ensure that: –

- The pharmaceutical products are designed and developed considering the requirement of GMP and other associated codes such as those of Good Laboratory Practices (GLP) and Good Clinical Practices (GCP);
- Adequate controls on starting materials, intermediate products, and bulk products and other in-process controls, calibrations and validations are carried out.
- The finished product is correctly processed and checked in accordance with established procedures;
- The pharmaceutical products are not released for sale or supplied before authorized persons have certified.

6.1.15 Self-Inspection and Quality Audit

It may be useful to constitute a self-inspection team supplemented with a quality audit procedure for assessment of all or part of a system with the specific purpose of improving it.

- To evaluate the manufacturer compliance with GMP in all aspects of production and quality control, concept of self-inspection shall be followed. The manufacturer shall constitute a team of independent, experienced, qualified persons from within or outside the organization, who can audit objectively the implementation of methodology and procedures evolved. The procedure for self-inspection shall be documented indicating self-inspection results; evaluation, conclusions and recommended corrective

actions with effective follow up program. The recommendations for corrective action shall be adopted.

- The program shall be designed to detect shortcomings in the implementation of Good Manufacturing Practice and to recommend the necessary corrective actions. Self-inspections shall be performed routinely and on specific occasions, like when product recalls or repeated rejections occur or when an inspection by the licensing authorities is announced. The team responsible for self-inspection shall consist of personnel who can evaluate the implementation of Good Manufacturing Practice objectively; all recommendations for corrective action shall be implemented.

6.1.16 Quality Control System

Quality control shall be concerned with sampling, specifications, testing, documentation, release procedures which ensure that the necessary and relevant tests are actually carried and that the materials are not released for use, nor products released for sale or supply until their quality has been judged to be satisfactory. It is not confined to laboratory operations but shall be involved in all decisions concerning the quality of the product. It shall be ensured that all quality control arrangements are effectively and reliably carried out by the department as a whole shall have other duties such as to establish evaluate, validate and implement all Quality Control Procedures and methods.

- Reference/retained samples from each batch of the products manufactured shall be maintained in quantity which is at least twice the quantity of the drug required to conduct all the tests, except sterility and pyrogen/Bacterial Endotoxin Test performed on the active material and the product manufactured. The retained product shall be kept in its final pack or simulated pack for a period of three months after the date of expiry.

- Assessment of records pertaining to finished products shall include all relevant factors, including the production conditions, the results of in process testing, the manufacturing (including packaging) documentation, compliance with the specification for the finished product and an

examination of the finished pack. Assessment records should be signed by the in-charge of production and countersigned by the authorised quality control personnel before a product is released for sale or distribution.

- Quality control personnel shall have access to production areas for sampling and investigation, as appropriate.
- The quality control department shall conduct stability studies of the products to ensure and assign their shelf life at the prescribed conditions of storage. All records of such studies shall be maintained.
- The in-charge of Quality Assurance shall investigate all product complaints and records thereof shall be maintained.
- All instruments shall be calibrated and testing procedures validated before these are adopted for routine testing. Periodical calibration of instrument and validation of procedures shall be carried out.
- Pharmacopoeia, reference standards, working standards, references, spectra, other reference materials and technical books, as required, shall be available in the Quality Control Laboratory of the licensee.

6.1.17 For Product Containers and Closures

- All containers and closures intended for use shall comply with the pharmacopoeial requirements. Suitable validated test methods, sample sizes, specifications, cleaning procedure and sterilization procedure, wherever indicated, shall be strictly followed to ensure that these are inert in nature. No second hand or used containers and closures shall be used.
- Whenever bottles are being used, the written schedule of cleaning shall be laid down and followed. Where bottles are not dried after washing, they should be rinsed with de-ionised water or distilled water, as the case may be.

6.1.18 Master Formula Records/Batch Packaging Records/ Batch Processing Records

Master formula records, Batch packaging records and Batch processing records shall include following:

Master Formula Records	Batch Packaging Records	Batch Processing Records
Name of the product together with product reference code relating to its specifications.	Name of the product	The name of the product and the number of the batch being manufactured.
The patent or proprietary name of the product along with the generic name, a description of the dosage form, strength, composition of the product and batch size.	Description of the dosage form, strength and composition.	Dates and time of commencement, of significant intermediate stages and of completion of production.
Name, quantity, and reference number of all the starting materials to be used and Statement of the expected final yield with the acceptable limits, and of relevant intermediate yields.	The pack size expressed in terms of the number of doses, weight or volume of the product in the final container.	Initials of the operator of different significant steps of production and where appropriate, of the person who checked each of these operations.
Processing location and the principal equipment to be used and Stepwise processing instructions and the time taken for each step.	Complete list of all the packaging materials required for a standard batch size, including quantities, sizes and types with the code of reference number relating to the specifications of each packaging material.	The batch number and/or analytical control number as well as the quantities of each starting material actually weighed.
Methods to be used for preparing the critical equipment including	Printed packaging materials and specimens indicating where batch	Relevant processing operation or event and major equipment used.

Master Formula Records	Batch Packaging Records	Batch Processing Records
cleaning, assembling, calibrating, sterilizing.	number and expiry date of the product have been applied.	
Instructions for in-process control with their limits.	Special precautions to be observed and line clearance.	A record of the in-process controls and the initials of the person carrying them out, and the results obtained.
Storage conditions of the products, including the container, labelling and special storage conditions.	Description of the packaging operation, including any significant subsidiary operations and equipment to be used.	Amount of product obtained after different and critical stages of manufacture (yield),and comments or explanations for significant deviations from the expected yield limits shall be given.
Any special precautions to be observed.	Details of in-process controls with instructions for sampling and acceptance.	Notes on special problems including details, with signed authorization, for any deviation from the Master Formula.
Packing details and specimen labels.	Reconciliation of labels.	Additional Information of any recovered or reprocessed material with reference to recovery or reprocessing stages.

6.1.19 Standard Operating Procedures (SOPs) and Records

Properly documented Standard Operating Procedures (SOP) and records for the each activities carried out shall be maintained, including SOP for receipt of each delivery of raw, primary, printed packaging material, internal labelling, quarantine and storage of starting materials, packaging materials, other materials, sampling which include the person(s) authorized to take the samples, each instrument and

equipment and these shall be placed in close proximity to the related instrument and equipment.

6.1.20 Batch Numbering

Standard operating procedures shall be maintained describing the details of the batch (lot) numbering set up with the objective of ensuring that each batch of intermediate, bulk or finished product is identified with a specific batch number.

Batch numbering standard operating procedures applied to a processing stage and to the respective packaging stage shall be same or traceable to demonstrate that they belong to one homogenous mix.

6.1.21 Records of Analysis

- The records shall include the following data:
  - Name of the material or product and the dosage form.
  - Batch number and where appropriate the manufacturer and/ or supplier.
  - Reference to the relevant specifications and testing procedures.
  - Test results, including observations and calculations, and reference to any specifications (limits).
  - Dates of testing.
  - Initials of the persons who performed the testing.
  - Initials of the persons who verified the testing and the detailed calculations.
  - Statement of release or rejection.
  - Signature and date of the designated responsible person.

- There shall be written standard operating procedures and the associated records of actions taken for:
  - Equipment assembly and validation.
  - Analytical apparatus and calibration.
  - Maintenance, cleaning and sanitation.
  - Personnel matters including qualification, training, clothing, hygiene.
  - Environmental monitoring.
  - Pest control.
  - Complaints.
  - Recalls.
  - Returns received.

6.1.22 Reprocessing and Recoveries

- Where reprocessing is necessary, written procedures shall be established and approved by the Quality Assurance department that shall specify the conditions and limitations of repeating chemical reactions. Such reprocessing shall be validated.
- If the product batch has to be reprocessed, the procedure shall be authorized and recorded. An investigation shall be carried out into the causes necessitating re-processing and appropriate corrective measures shall be taken for prevention of recurrence. Re-processed batch shall be subjected to stability evaluation.
- Recovery of the product residue may be carried out, if permitted, in the master production and control records by incorporating it in subsequent batches of the product.

6.1.23 Distribution Records

- Prior to distribution or dispatch of given batch of a drug, it shall be ensure that the batch has been duly tested, approved and released by the quality control personnel.
- Pre-dispatch inspection shall be performed on each consignment on a random basis to ensure that only the correct goods are dispatched.
- Detailed instructions for warehousing and stocking of Large Volume Parenteral, if stocked, shall be in existence and shall be complied with after the batch is released for distribution.

6.1.24 Validation and Process Validation

- Validation studies shall be an essential part of Good Manufacturing Practices and shall be conducted as per the pre-defined protocols. These shall include validation of processing, testing and cleaning procedures.
- A written report summarizing recorded results and conclusions shall be prepared, documented and maintained.
- Processes and procedures shall be established on the basis of validation study and undergo periodic revalidation to ensure that they remain capable of achieving the intended results. Critical processes shall be validated, prospectively for retrospectively.
- When any new master formula or method of preparation is adopted, steps shall be taken to demonstrate its suitability for routine processing. The defined process, using the materials and equipment specified shall be demonstrated to yield a product consistently of the required quality.
- Significant changes to the manufacturing process, including any changes in equipment or materials that may affect product quality and/or the reproducibility of the process, shall be validated.

6.1.25 Product Recalls

- A prompt and effective product recall system of defective products shall be devised for timely information of all concerned stockists, wholesalers, suppliers, up to the retail level within the shortest period. The licensee may make use of both print and electronic media in this regard.
- There shall be an established written procedure in the form of standard operating procedure for effective recall of products distributed by the licensee. Recall operations shall be capable of being initiated promptly so as to effectively reach at the level of each distribution channel.
- The distribution records shall be readily made available to the persons designated for recalls.
- The designated person shall record a final report issued, including reconciliation between the delivered and the recovered quantities of the products.
- The effectiveness of the arrangements for recalls shall be evaluated from time to time.
- The recalled products shall be stored separately in a secured segregated area pending final decision on them.
- Mock Recall to be performed to evaluate effectiveness of established recall procedure.

6.1.26 Complaints and Adverse Reactions

- All complaints thereof concerning product quality shall be carefully reviewed and recorded according to written procedures. Each complaint shall be investigated /evaluated by the designated personnel of the organization and records of investigation and remedial action taken thereof shall be maintained.

- Reports of serious adverse drug reactions resulting from the use of a drug along with comments and documents shall be forthwith reported to the concerned licensing authority.

  There shall be written procedure describing the action to be taken and recall to be made of the defective product.

6.1.27 Site Master File

The licensee shall prepare a succinct document in the form of Site Master File containing specific and factual GMP about the production and/or control of pharmaceutical manufacturing preparations carried out at the licensed premises.

It shall contain the following: –

Content	Description
General information	– Brief information of the entity. – Manufacturing activities as permitted by the licensing authority. – Flow charts mentioning procedure and process flow. – Number of employees engaged in various departments. – Use of outside scientific, analytical or other technical assistance in relation to manufacture and analysis. – Short description of the Quality Management System of the firm. – Products details registered with foreign countries.
Personnel	– Organisational chart. – Qualification, experience and responsibilities of key personnel. – Outline for arrangements training and how the records are maintained. – Personal hygiene requirements, including clothing.
Premises	– Simple plan or description of manufacturing areas drawn to scale. – Nature of construction and fixtures/fittings.

Content	Description
	– Brief description of ventilation systems. – Areas for the handling of the highly toxic, hazardous and sensitizing materials. – Water system (schematic drawings of systems), including sanitation. – Preventive maintenance programs.
Equipment	– A list of equipment. – Qualification and calibration including the recording systems and arrangements for computerized systems validation.
Sanitation	– Specifications and procedures for cleaning manufacturing areas and equipment.
Documentation	– Arrangements for the preparation, revision and distribution. – Necessary documentation for the manufacture. – Documentation related to product quality that is not mentioned elsewhere (e.g. microbiological controls about air and water).
Production	– Brief description of production operations using with flow sheets and charts. – Arrangements for the handling of starting materials, packaging materials, bulk and finished products, including sampling, quarantine, release and storage. – Arrangements for the handling of rejected materials and products. – Brief description of general policy for process validation.
Quality Control	– Description of the quality control system and of the activities. – Procedures for the release of the finished products.
Loan licence manufacture and licensee	– Description of the way in which compliance of Good Manufacturing Practices by the loan licensee shall be assessed.
Distribution, complaints and product recall	– Arrangements and recording system for distribution. – Arrangements for handling of complaints and product recalls.

Content	Description
Self–inspection	– Short description of the self–inspection system indicating whether an outside, independent and experienced external export was involved in evaluating the manufacturers' compliance with Good Manufacturing Practices in all aspects of production.
Export of drugs	– Products exported to different countries. – Complaints and product recall, if any.

6.2 Specific Requirements for Other Pharmaceutical Formulations

Apart from general requirements,Schedule M describes some specific requirements as below:–

1. Manufacture of sterile products, parenteral preparations (small volume injectable and large volume parenteral) and sterile ophthalmic preparations.
2. Manufacture of oral solid dosage forms (tablets and capsules).
3. Manufacture of oral liquids (syrups, elixirs, emulsions and suspensions).
4. Manufacture of topical products i.e. Topical preparations (creams, ointments, pastes, emulsions, lotions, solutions, dusting powders and identical products).
5. Manufacture of metered–dose–inhalers. Premises, plant and materials for manufacture of active pharmaceutical ingredients (bulk drugs).

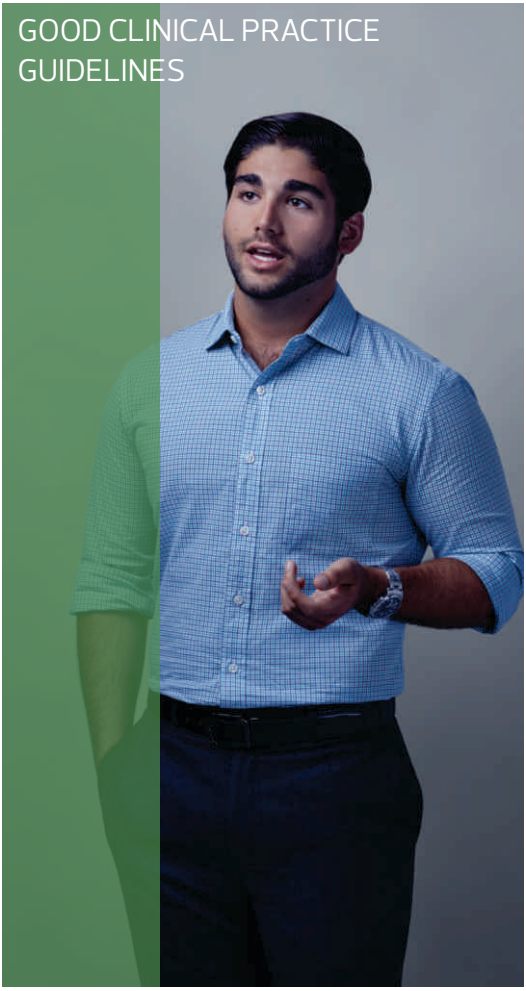
6.3 Specific Requirements of Other Organizations

Schedule M also prescribes specific requirements of factory premises for the manufacture of other branches of pharmacy such as:

- Homeopathic preparations
- Cosmetics
- Medical devices

Chapter 7

GOOD CLINICAL PRACTICE GUIDELINES



Chapter 7 Good Clinical Practice Guidelines

7.1 Background

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected; consistent with the principles that have their origin in the Declaration of Helsinki (set of ethical principles regarding human experimentation developed for the medical community by the World Medical Association), and that the clinical trial data are credible.

7.2 Investigator

Investigators are the individuals or institutes who conduct clinical trials according to approved protocols and GCP guidelines.

Investigators are responsible for compliance as per the undertaking given in Appendix VII in Drug And Cosmetic Act 1945, Schedule Y. Standard operating procedures are required to be documented by the investigators for the tasks performed by them. During and following a subject's participation in a trial, the investigator should ensure that adequate medical care is provided to the participant for any adverse events. Investigators shall report all serious and unexpected adverse events to the Sponsor within 24 hours and to the Ethics Committee that accorded approval to the study protocol within 7 working days of their occurrence.

7.3 Sponsor

Sponsors are the individuals or institutes who are implement and maintain quality system to ensure that the clinical trials are conducted in accordance with the approved protocols and GCP guidelines.

Sponsors are required to submit a status report on the clinical trial to the Licensing Authority within the prescribed periodicity.

In case of studies prematurely discontinued for any reason including lack of commercial interest in pursuing the new drug application, a summary report should be submitted within 3 months. The summary report should provide a brief description of the study, the number of patients exposed to the drug, dose and duration of exposure, details of adverse drug reactions (Appendix XI, Drug And Cosmetic Act 1945), if any, and the reason for discontinuance of the study or on-pursuit of the new drug application.

Any unexpected serious adverse event (SAE). (As defined in GCP Guidelines) occurring during a clinical trial should be communicated promptly (within 14 calendar days) by the Sponsor to the Licensing Authority and to the other Investigator(s) participating in the study (see Appendix XI of Drug And Cosmetic Act 1945, schedule Y).

For detailed requirement for GCP compliance refer Drugs And Cosmetic Act 1945, Schedule Y.

(http://www.cdsco.nic.in/writereaddata/Drugs&CosmeticAct.pdf)

Chapter 8

VARIOUS INTERNATIONAL LAWS

Chapter 8 Various International Laws

8.1 WHO Medicines

WHO guidelines deal with medicines policy, intellectual property rights, financing & supply management, quality & safety, selection & rational use of medicines, technical co-operation and traditional medicines. Some of the guidelines are mentioned below.

8.1.1 Good Manufacturing Practices

As explained herein before in earlier chapter, GMP is that part of quality management which ensures that products are consistently produced and controlled according to the quality standards appropriate to their intended use and as required by the marketing authorization, clinical trial authorization or product specification. GMP is concerned with both production and QC.

8.1.2 Good Pharmacy Practice

It is the policy of FIP and WHO to provide guidance to national pharmacy professional organizations regarding the development of their national GPP guidelines. The conditions of practice vary widely from country to country. To support this practice it is essential that there be an established national framework of quality standards and guidelines.

- GPP requires that a pharmacist's first concern in all settings is the welfare of patients.
- GPP requires that the core of the pharmacy activity is to help patients make the best use of medicines. Fundamental functions include the supply of medication and other health-care products of assured quality, the provision of appropriate information and advice to the patient, administration of medication, when required, and the monitoring of the effects of medication use.
- Pharmacists should have input into decisions about the use of medicines.
- A system should exist that enables pharmacists to report and to obtain

feedback about adverse events, medicine-related problems, medication errors, misuse or medicine abuse, defects in product quality or detection of counterfeit products.

- The pharmacist should be aware of essential medical and pharmaceutical information (i.e. diagnosis, laboratory test results and medical history)about each patient. The pharmacist needs evidence-based, unbiased, comprehensive, objective and current information about therapeutics, medicines and other healthcare products in use, including potential environmental hazard caused by disposal of medicines' waste.

- National standards of GPP should be specified and should be adhered to by practitioners.

- At the national or appropriate (e.g. state or provincial) level, it is necessary to establish a legal framework that defines who can practice pharmacy; defines the scope of pharmacy practice; and ensures the integrity of the supply chain and the quality of medicines.

8.1.3 Data and Record Management

GDRP (Good Documentation Record Practice) are critical elements of the pharmaceutical quality system and a systematic approach should be implemented to provide a high level of assurance that throughout the product life cycle, all GXP (good (anything) practice) records and data are complete and reliable.

The data governance programme should include policies and governance procedures that address the general principles listed below for a good data management programme. These principles are clarified with additional detail in the sections below:

- **Applicability to both paper and electronic data:** The requirements for GDRP that assure robust control of data validity apply equally to paper and electronic data.

- **Applicability to contract givers and contract acceptors:** The principles of

these guidelines apply to contract givers and contract acceptors. Contract givers are ultimately responsible for the robustness of all decisions made on the basis of GXP data.

- **Good documentation practices:** To achieve robust decisions, the supporting data set needs to be reliable and complete. GDP should be followed in order to ensure all records, both paper and electronic, allow the full reconstruction and traceability of GXP activities.

- **Management governance:** To establish a robust and sustainable good data management system it is important that senior management ensures that appropriate data management governance programmes are in place. Elements of effective management governance should include:

  - application of modern QRM principles and good data management principles that assure the validity, completeness and reliability of data;

  - application of appropriate quality metrics.

- **Quality culture:** Management, with the support of the quality unit, should establish and maintain a working environment that minimizes the risk of non-compliant records and erroneous records and data. An essential element of the quality culture is the transparent and open reporting of deviations, errors, omissions and aberrant results at all levels of the organization, irrespective of hierarchy.

- **Quality risk management and sound scientific principles:** Robust decision making requires appropriate quality and risk management systems and adherence to sound scientific and statistical principles, which must be based upon reliable data.

- **Data life cycle management:** Continual improvement of products to ensure and enhance their safety, efficacy and quality requires a data governance approach to ensure management of data integrity risks throughout all

phases of the process by which data are created, recorded, processed, transmitted, reviewed, reported, archived and retrieved.

- To ensure that the organization, assimilation and analysis of data into a format or structure that facilitates evidence-based and reliable decision making, data governance should address data ownership and accountability for data process(es) and risk management of the data life cycle.

8.1.4 Documentation

- **Documentation in case of Biological products**

  - In general, the processing records of regular production batches should provide a complete account of the manufacturing activities of each batch showing that it has been produced, tested and dispensed into containers in accordance with the approved procedures.

  - In the case of vaccines, a batch processing record and a summary protocol should be prepared for each batch for the purpose of lot release by the NRA. The information included in the summary protocol should follow the WHO Guidelines for independent lot release of vaccines by regulatory authorities. The summary protocol associated records should be of a type approved by the NRA.

  - Manufacturing batch records should be retained for at least 1 year after the expiry date of the batch starting materials may require additional documentation on source, origin, supply chain, method of manufacture and controls applied.

- **Documentation in case of Blood Establishments**

Standard operating procedures and records	Document control and Document management	Record retention and archiving
Standard operating procedures : - Purchase and receipt	- All documents should be laid out in an orderly manner with a	- All records, including raw data, which are critical to the safety

Standard operating procedures and records	Document control and Document management	Record retention and archiving
of starting materials – Selection of donors – Collection of blood – Preparation of blood components – Laboratory testing and associated quality control testing – Product labelling, storage release, dispatch, shipping – Recall of final products **Records:** – Each activity that may affect the quality of blood and blood components should be documented and recorded at the time it takes place. – Critical activities should be double-checked, either by a second person or electronically. – Critical manufacturing and laboratory testing records should be reviewed frequently for completeness, legibility and, when appropriate, accuracy by the manager or	unique title and reference number, and should indicate the version and the effective date. – The content of the document should be clear and should not include superfluous information. – Title, nature, purpose and scope should be clearly outlined. – Documents should be reviewed, approved, signed and dated by authorized persons. – An audit trail should indicate the person responsible for each step of document control. **Controls** – A document control standard operating procedure should be established for the development, review, approval, distribution, implementation, revision and archival of documents. – There should be a record of the distribution of each	and quality of blood or blood components, should be kept in a secured storage area according to national regulations, or preferably for at least 10 years. – A longer period for retention of records may be required by NRAs, international requirements or by specific contractual agreements. Records of permanently deferred donors should be kept indefinitely.

Standard operating procedures and records	Document control and Document management	Record retention and archiving
other designated person.	document which also shows at least the work areas or tasks affected by the document.	

- Documentation system and specifications for Intermediates or Active Pharmaceutical Ingredients

  - All documents should be prepared, reviewed, approved and distributed according to written procedures. Such documents can be in paper or electronic form.
  - The issuance, revision, superseding and withdrawal of all documents should be controlled with maintenance of revision histories.
  - A procedure should be established for retaining all appropriate documents the retention periods for these documents should be specified.
  - For APIs with retest dates, records should be retained for at least three years after the batch is completely distributed.
  - Entries in records should be made indelibly in spaces provided for such entries, directly after performing the activities, and should identify the person making the entry. Corrections to entries should be dated and signed ensuring that the original entry remains readable.
  - Specifications should be established and documented for raw materials, intermediates where necessary, APIs and labelling and packaging materials. Acceptance criteria should be established and documented for in-process controls.

- If electronic signatures are used on documents they should be authenticated and secure.

8.2 WHO Sites

WHO guidelines on all areas relevant to health of people all over, some of the areas are discussed below:

Vaccine Standardization	– General guidelines on technical or regulatory topics such as cell substrates, nonclinical evaluation, or clinical evaluation. – Establishes and distributes the WHO Biological Reference Materials required for the standardization of assays.
Medical Quality assurance	Contributes to public health by enabling quality medicines to reach patients through:– – developing norms, standards and guidelines for quality assurance – developing the international pharmacopoeia – establishing International Chemical Reference Substances (ICRS) – collaborating with numerous stakeholders – providing country support
Medicine Safety	The minimum requirements were developed through an interactive process involving – Face to face meeting of pharmacovigilance practitioners, disease control managers, technical agencies and donors. – discussion of the proposed minimum requirements document by the World Health Organization's Advisory Committee on the Safety of Medicinal Products – consolidation of all views and comments and production of the Draft Minimum Requirements Document for wider stakeholder consultation
Drug Resistance	– New guidelines on use of medically important antimicrobials in food-producing animals, recommending that farmers and the food industry stop using antibiotics routinely to promote growth and prevent disease in healthy animals. – Aim to help preserve the effectiveness of antibiotics that are important for human medicine by reducing their use in animals

8.3 Organisation for Economic Co-operation and Development (OECD)

The mission of the OECD is to promote policies that will improve the economic and social well-being of people around the world.

OECD provides a forum in which governments can work together to share experiences and seek solutions to common problems.

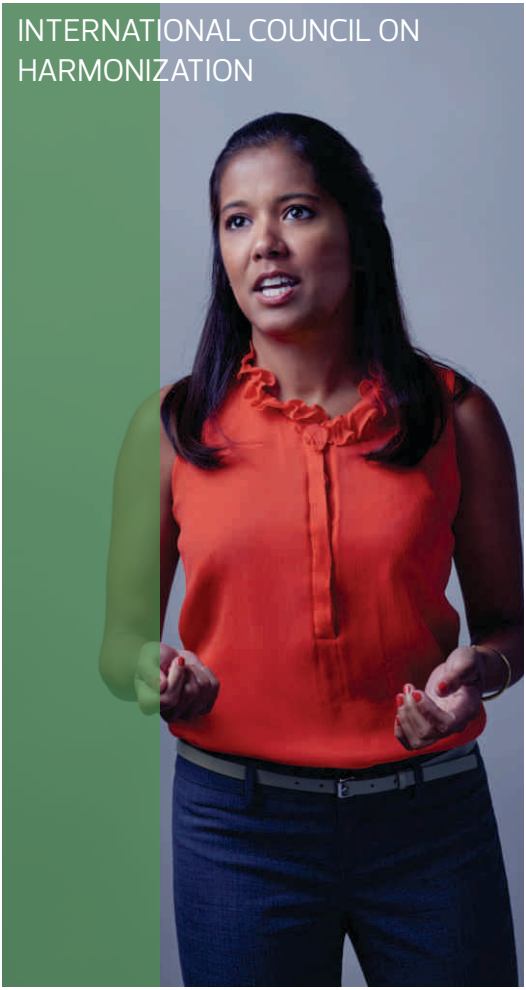
8.4 Therapeutic Goods Administration (TGA)

The Therapeutic Goods Administration (TGA), as part of the Department of Health, protects the health and wellbeing of the community by regulating and monitoring all therapeutic goods that are distributed in Australia. Hence if an Indian organization exports drugs to Australia, it shall need to comply with this standard.

TGA regulates the supply of all types of medicine, medicaldevices, diagnostic products, vaccines and blood products.TGA also regulates manufacturing and advertising of such products.

Chapter 9

INTERNATIONAL COUNCIL ON HARMONIZATION



Chapter 9 International Council on Harmonization

The International Council for Harmonisation (ICH) of technical requirements for pharmaceuticals for human use is unique in bringing together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of drug registration. ICH issues quality guidelines, safety guidelines, efficiency guidelines and Multi-disciplinary guidelines which are discussed below:

ICH topics are divided in to four topics:

1. Quality Guidelines
2. Safety Guidelines
3. Efficacy Guidelines
4. Multidisciplinary Guidelines

9.1 Quality Guidelines

Harmonisation achievements in the quality area include pivotal milestones such as the conduct of stability studies, defining relevant thresholds for impurities testing and a more flexible approach to pharmaceutical quality based on GMP risk management.

Quality Guidelines involves following topics:

Sr. No.	Guidelines	Description
1.	Q1	Stability Study
	Q1A(R2)	Stability testing of new drug substances and products
	Q1B	Photo Stability Testing of New Drug Substances and Products
	Q1C	Stability Testing for New Dosage Forms
	Q1D	Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products
	Q1E	Evaluation of Stability Data
	Q1F	Stability Data Package for Registration Application in Climatic Zones III and IV
2.	Q2R1	Validation of analytical procedures
3.	Q3	Impurities
	Q3A (R2)	Impurities in New Drug Substances

Sr. No.	Guidelines	Description
	Q3B (R2)	Impurities in New Drug Products
	Q3C (R5)	Guideline for Residual Solvents
	Q3D	Guideline for Elemental Impurities
4.	Q4	Pharmacopoeias
	Q4B Annex 1(R1)	Residue on Ignition / Sulphated Ash General Chapter
	Q4B Annex 2(R1)	Test for Extractable Volume of Parenteral Preparation General Chapter
	Q4B Annex 3(R1)	Test for Particulate Contamination : Sub-Visible Particles General Chapter
	Q4B Annex4A(R1)	Microbiological Examination of Non-Sterile Products : Microbial Enumeration Tests General Chapter
	Q4B Annex4B(R1)	Microbiological Examination of Non-Sterile Products : Test for Specified Micro-Organism General Chapter
	Q4B Annex4C(R1)	Microbiological Examination of Non-Sterile Products : Acceptance Criteria for Pharmaceutical Preparations and Substances for Pharmaceutical use General Chapter
	Q4BAnnex 5(R1)	Disintegration Test General Chapter
	Q4B Annex 6 (R1)	Uniformity of Dosage Units General Chapter
	Q4B Annex 7(R2)	Dissolution Test General Chapter
	Q4B Annex 8(R1)	Stability Test General Chapter
	Q4B Annex 9(R1)	Tablet Friability General Chapter
	Q4BAnnex 10(R1)	Polyacrylamide Gel Electrophoresis General Chapter
	Q4B Annex 11	Capillary Electrophoresis General Chapter
	Q4B Annex 12	Analytical Sieving General Chapter
	Q4B Annex 13	Bulk Density and Tapped Density of Powders General Chapter
	Q4B Annex 14	Bacterial Endotoxin Test General Chapter

Sr. No.	Guidelines	Description
5.	Q5	Quality of biological products
	Q5A(R1)	Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin
	Q5B	Quality of Biotechnology Products
	Q5D	Derivation and Characterisation of Cell Substrates used for Production of Biotechnological/Biological Products
	Q5E	Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process
6.	Q6	Specifications
	Q6A	Test Procedure and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances
	Q6B	Test Procedure and Acceptance Criteria for Biotechnological/Biological
7.	Q7	Good manufacturing practices of API
8.	Q8	pharmaceutical development
9.	Q9	Quality risk management
10.	Q10	Pharmaceutical quality system
11.	Q11	Development and manufacture of drug substances
12.	Q12	Lifecycle management

9.2 Safety Guidelines

ICH has produced a comprehensive set of safety guidelines to uncover potential risks like carcinogenicity, genotoxicity and reprotoxicity. A recent breakthrough has been a non-clinical testing strategy for assessing the QT interval prolongation liability: the single most important cause of drug withdrawals in recent years. Some guidelines related to Pharmaceuticals are described below:

Sr. No.	Guidelines	Description
1.	S1A–S1C	Carcinogenicity
2.	S2	Non-toxicity
3.	S3A–S3B	Toxic kinetics and pharmacokinetics
4.	S4	Toxicity testing

Sr. No.	Guidelines	Description
5.	S5	Reproductive toxicology
6.	S6	Biotechnology products
7.	S7A–S7B	Pharmacology Study
8.	S8	Immunotoxicology study
9.	S9	Nonclinical evaluation for anticancer activities
10.	S10	Photo safety Evaluation
11.	S11	Nonclinical paediatric study

9.3 Efficacy Guidelines

The work carried out by ICH under the Efficacy heading is concerned with the design, conduct, safety and reporting of clinical trials. It also covers novel types of medicines derived from biotechnological processes and the use of pharmacogenetics/ pharmacogenomics techniques to produce better targeted medicines. Some guidelines are described below:

Sr. No.	Guidelines	Description
1.	E1	Clinical Safety for Drugs used in Long-Term Treatment.
2.	E2A–E2F	Pharmacovigilance
3.	E3	Clinical Study Reports
4.	E4	Dose-Response Studies
5.	E5	Ethnic Factors
6.	E6	Good Clinical Practice
7.	E7	Clinical Trials in Geriatric Population
8.	E8	General Considerations for Clinical Trials
9.	E9	Statistical principle of clinical trials
10.	E10	Choice of control group for clinical trials
11.	E11	Clinical trials for paediatric population
12.	E12	Clinical evaluation by therapeutic category
13.	E14	Clinical evaluation for QT
14.	E15	Definitions for pharmacokinetics
15.	E16	Qualification for Genomic biomarkers
16.	E17	Multiregional clinical trials

Sr. No.	Guidelines	Description
17.	E18	Genomic sampling
18.	E19	Safety data collection

9.4 Multidisciplinary Guidelines

Those are the cross-cutting topics which do not fit uniquely into one of the Quality, Safety and Efficacy categories. It includes the ICH medical terminology (MedDRA), the Common Technical Document (CTD) and the development of Electronic Standards for the Transfer of Regulatory Information (ESTRI).

Sr. No.	Guidelines	Description
1.	M1	MedDRA Technology
2.	M2	Electronic standards
3.	M3	Non Clinical safety studies
4.	M4	Common Technical documents
5.	M5	Data elements and Standards for drug dictionary
6.	M6	Gene therapy
7.	M7	Genotoxic impurities
8.	M8	Electronic common technical documents
9.	M9	Bio pharmaceutics classifications
10.	M10	Bio analytical method validation

Chapter 10

EUROPEAN MEDICINES AGENCY (EMEA)

Chapter 10 European Medicines Agency (EMEA)

The European Medicines Agency (EMA) presents information on regulatory topics in the three main stages of the medicinal product lifecycle, to help users find information as easily as possible. It contains three main sections corresponding to the key medicinal product life cycle stages i.e. Research and Development, Marketing authorisation and Post authorisation. Some of the guidelines are described below:

10.1 Compliance

All organisations involved in the development, marketing, manufacture and distribution of medicines in European market are responsible for ensuring that they comply with all relevant standards set out in European Union (EU) legislation and guidelines on pharmaceuticals.

Any manufacturer of medicines intended for the EU market, irrespective of its location, must comply with GMP. GMP requires that medicines are of consistent high quality; are appropriate for their intended use; meet the requirements of the marketing authorisation or clinical trial authorisation. Most of the GMP requirements of EMEA are similar to the general GMP as discussed in earlier chapter on GMP. However, EMEA lays extensive emphasis on the following Quality Risk Management Processes.

The Quality Risk Management process should be the basis for determining the extent of technical and organisational measures required to control risks for cross-contamination. These could include, technical measures (premises and equipment, process design, utility design and prevention of contamination) and organisational measures (facility, maintenance, monitoring of risk and environmental aspects and handling of deviations and incidents)

10.2 Quality Control

The independence of quality control from production is considered fundamental to the satisfactory operation of quality control.

All analytical operations must follow clearly defined procedures; they must comply with the principles of good laboratory practice and ICH requirements as described

in other chapters of this publication. Apart from this, EMEA also requires all analytical methods to be validated as per "European Pharmacopoeia".

- **Regarding Outsourced Activities:**
    - There should be a written contract covering the outsourced activities, the products or operations to which they are related and any technical arrangements made in connection with it.

10.3 Transportation Validation

Apart from the GMP requirements, EMEA requires transportation system verification. The European commission has launched the revised Annex 15 (Qualification and Validation) on verification of transportation systems. It includes the study of risk assessement of impact of temperature, humidity, vibration and material handling.

Chapter 11

CODE OF FEDERAL REGULATIONS– TITLE 21 – US FDA

Chapter 11 Code of Federal Regulations– Title 21 – US FDA

Title 21 is the portion of the Code of Federal Regulations that governs food and drugs within the United States for the Food and Drug Administration (FDA), the Drug Enforcement Administration (DEA), and the Office of National Drug Control Policy (ONDCP).

11.1 US FDA covers below topics (21 CFR)

Chapter I	Food and drug administration, department of health and human services (Parts 1 – 1299).
Subchapter A	General (parts 1 – 99)
Subchapter B	Food for human consumption (parts 100 – 199)
Subchapter C	Drugs: general (parts 200 – 299)
Part 200	General
Part 201	Labelling
Part 202	Prescription drug advertising
Part 203	Prescription drug marketing
Part 205	Guidelines for state licensing of wholesale prescription drug distributors
Part 206	Imprinting of solid oral dosage form drug products for human use
Part 207	Registration of producers of drugs and listing of drugs in commercial distribution
Subpart A	General
Subpart B	Exemptions
Subpart C	Procedures for Domestic Drug Establishments
Section 207.20	Who must register and submit a drug list
Section 207.21	Times for registration and drug listing
Section 207.22	How and where to register and list drugs
Section 207.25	Information required in registration and drug listing
Section 207.26	Amendments to registration
Section 207.30	Updating drug listing information
Section 207.31	Additional drug listing information

Section 207.35	Notification of registrant; drug establishment registration number and drug listing number
Section 07.37	Inspection of registrations and drug listings
Section 207.39	Misbranding by reference to registration or to registration number
Subpart D	Procedure for Foreign Drug Establishments
Part 208	Medication guides for prescription drug products
Part 209	Requirement for authorized dispensers and pharmacies to distribute a side effects statement
Part 210	Current good manufacturing practice in manufacturing, processing, packing, or holding of drugs
Part 211	Current good manufacturing practice for finished pharmaceuticals
Part 212	Current good manufacturing practice for positron emission tomography drugs
Part 216	Pharmacy compounding
Part 225	Current good manufacturing practice for medicated feeds
Part 226	Current good manufacturing practice for type a medicated articles
Part 250	Special requirements for specific human drugs
Part 290	Controlled drugs
Part 299	Drugs; official names and established names
Subchapter D	Drugs for human use (parts 300 – 499)
Subchapter E	Animal drugs, feeds, and related products (parts500 – 599)
Subchapter F	Biologics (parts 600 – 680)
Subchapter G	Cosmetics (parts 700 – 799)
Subchapter H	Medical devices (parts 800 – 898)
Subchapter I	Mammography quality standards act (part 900
Subchapter J	Radiological health (parts 1000 – 1050)
Subchapter K	Tobacco products (part 1140)
Subchapter L	Regulations under certain other acts administered by the food and drug administration (parts 1210 –1299)
Chapter II	Drug enforcement administration, department of justice (parts 1300 – 1321)
Chapter III	Office of national drug control policy (parts 1400 – 1499)

11.2 Registration

- Foreign drug establishments whose drugs are imported or offered for import into the United States are required to register with FDA and submit listing information for their drugs intended for commercial distribution in the United States.

- Additionally, if the foreign manufacturer has not previously registered, they are required to register with the FDA within 5 days after submitting a drug application, biological license application, or medicated feed mill license application.

- These regulations also require importers to identify a U.S. Agent. Registration and Listing must be completed electronically with CDER unless a waiver from the electronic submission requirement is obtained.

- With certain exemptions, any establishment engaged in the manufacture, repacking, relabeling, or salvaging of a drug product for commercial distribution is required to register with FDA.

  Some exemptions include (but not limited to):

  1. Pharmacies that:

     a. Operate in conformance with all applicable local laws regulating the practice of pharmacy and medicine;

     b. Regularly engage in dispensing prescription drugs upon a valid prescription; and

     c. Do not manufacture, repack, relabel, or salvage drugs other than in the regular course of their business of dispensing or selling drugs at retail.

  2. Hospitals, clinics, other health care entities, and public health agencies that:

a. Operate establishments in conformance with all applicable local laws regulating the practice of pharmacy and medicine;

b. Regularly engage in dispensing prescription drugs upon a valid order or prescription;

c. Do not manufacture, repack, re-label, or salvage drugs other than in the regular course of their practice of pharmacy, including dispensing;

3. Practitioners who are licensed by law to prescribe or administer drugs and who manufacture, repack, re-label, or salvage drugs solely for use in their professional practice;

4. Manufacturers, re-packers, re-labellers, or salvagers who manufacture, repack, relabel, or salvage drugs solely for use in research, teaching, or chemical analysis and not for sale;

5. Manufacturers, re-packers, and re-labellers of harmless inactive ingredients such as excipients, colourings, flavourings, emulsifiers, lubricants, preservatives, or solvents that become components of drugs;

6. Carriers, in their receipt, carriage, holding, or delivery of drugs in the usual course of business as carriers;

7. Storage facilities which do not perform any manufacturing function.

11.3 Listing

- All registered establishments must list all of the products they produce for commercial distribution under their own labeller code. This includes API manufacturers, other bulk manufacturers, contract manufacturers, re-packers, and re-labellers.

- Data need to list a product under FDA:-

- Full 10-digit NDC;
- Proprietary and non-proprietary name (generic drugs may use the non-proprietary name for both);
- Dosage form and route of administration;
- The name (with unique ingredient identifier or UNII code) and amount/strength (with appropriate unit of measure e.g. grams, millilitres, etc.) of each active ingredient;
- Each inactive ingredient (name and UNII) only;
- A copy of the most up-to-date labelling, including a JPG file of the outer packaging and principal display panel;
- The name and DUNS number for each establishment involved in manufacturing the product.

– Blanket No Change Certification for Product Listing Data

- The period for Product Listing Certification using the Product Listing Certification SPL submission is October 1st through December 31st. Any product listing that is required to be certified but not certified, may be considered inactive and removed from the NDC Directory and other publications of listing data. Outside this three month window an update of the Listing SPL submission for each NDC is required to certify the product.

– Use of the National Drug Code

- An NDC is the unique identifier for drugs in the United States. Assignment of NDC to non-drugs is not permitted. Therefore, NDCs should not be assigned to non-drug products, such as medical devices and medical foods. Inclusion of the NDC on some drug labels may not be required, but if included, it must follow the required

format and applicable labeling rules. Submission of NDC is required at the time of drug listing with FDA.

- FDA conducts field examinations and analyses samples of drug products to ensure they comply with applicable standards and/or label requirements

- FDA requires that all drugs in the United States be shown to be both safe and effective prior to marketing.

- NDA (New Drug Application)

  Every new drug must have an approved NDA before becoming available for sale in the United States.

- ANDA (Abbreviated New Drug Application)

  The ANDA contains data which provides for the review and ultimate approval of a generic drug product.

- IND (Investigational New Drug)

  FDA requires that certain drugs be the subject of an approved marketing application (NDA/ANDA) before it is offered for importation into the United States. To submit a marketing application for approval, data must be gathered during animal and human clinical trials. A sponsor must seek an exemption from this legal requirement in order to import the drug for these clinical trials. The IND is the means through which the sponsor technically obtains this exemption from the FDA.

- Drug Labelling

  All drug products offered for importation into the United States are subject to labelling requirements. Specific drug labelling requirements depend on the type of drug product. Over—the-counter drugs, prescription drugs, and drugs imported for drug efficacy studies are subject to specific labelling requirements in addition to the general drug label provisions.

- Affirmations of Compliance codes for human drugs
- Affirmations of Compliance codes (A of C) are three letter codes that can be provided at the time of import to facilitate FDA review.
- Providing the correct A of C codes reduces the likelihood that your shipment will be held for further FDA entry review during FDA's import screening process. FDA uses A of C codes to assist in verifying that your product meets the appropriate requirements. Submission of A of C codes is only mandatory in some instances and is not required for all scenarios. Submitting voluntary A of C codes in addition to all mandatory A of C codes may expedite initial screening and review of your entry.
- A general requirement of systems for controlling the manufacture of drugs and drug products consists of the following:

Quality System	• It assures overall compliance with CGMPs and internal procedures and specifications. This system includes the quality control unit and all of its review and approval duties It includes all product defect evaluations and evaluation of returned and salvaged drug products.
Facilities and Equipment System	Measures and activities which provide an appropriate physical environment and resources used in the production of the drugs or drug products, It includes:– • Buildings and facilities along with maintenance; • Equipment qualifications (installation and operation) • Equipment calibration and preventative maintenance; • Cleaning and validation of cleaning processes as appropriate.
Materials System	• Measures and activities to control finished products, components, including water or gases that are incorporated into the product, containers and closures. • Validation of computerized inventory control processes, drug storage, distribution controls, and records.

Production System	• Measures and activities to control the manufacture of drugs and drug products including batch compounding, dosage form production, in-process sampling and testing, and process validation. • Establishing, following, and documenting performance of approved manufacturing procedures.
Packaging and Labelling System	• Measures and activities that control the packaging and labelling of drugs and drug products. It includes written procedures, label examination and usage, label storage and issuance, packaging and labelling operations controls, and validation of these operations.
Laboratory Control System	• Measures and activities related to laboratory procedures, testing, analytical methods development and validation or verification, and the stability program.

11.4 General Enforcement Regulations

General Enforcement regulation includes various controls and legislation in following activities:

Labelling	Imports and exports
Consequences of failing to register, update, renew, or cancel registration Imports and exports	Consequences of failing to register, update, renew, or cancel registration Good laboratory practice for non-clinical laboratory studies
Colour additives	General provisions for Manufacturer and distributes
Imprinting of solid oral dosage form drug products for human use	Good laboratory practice for non-clinical laboratory studies

11.5 Requirements for foreign and domestic establishment registration and listing for human drugs, including drugs that are regulated under Biologics License Application, Animal Drugs and the National Drug Code

This part applies to:

- Domestic manufacturers, domestic re-packers, domestic re-labellers and domestic salvagers, not exempt under section 510(g) of the Federal Food, Drug, and Cosmetic Act or 207.13, regardless of whether their drugs enter interstate commerce.

- Foreign manufacturers, foreign re-packers, foreign re-labellers and foreign salvagers, not exempt under section 510(g) of the Federal Food, Drug, and Cosmetic Act or 207.13.

- Private label distributors, because they must have labeller codes.

- Establishments engaged in the manufacture, repacking, relabeling, or salvaging of human drugs regulated under a biologics license application (BLA). These establishments are subject to the requirements of this part unless they are required to register and list such drugs as human blood or blood products under part 607 of this chapter and do not engage in activities that would otherwise require them to register and list under this part.

- Establishments engaged in the manufacture (as defined in 1271.3(e) of this chapter) of human cells, tissues, and cellular and tissue-based products (HCT/Ps) (as defined in 1271.3(d) of this chapter) that, under 1271.20 of this chapter, are also drugs regulated under section 351 of the Public Health Service Act or section 505 of the Federal Food, Drug, and Cosmetic Act. These establishments must register and list that HCT/Ps following the procedures described in this part.

- One may refer https://www.fda.gov/ for detailed registration requirements. refer:-

Annexure 1 DTAA Rate Chart

DTAA RATE CHART*

Country	Dividend	Interest	Royalty	FTS
Albania	10%	10%	10%	10%
Armenia	10%	10%	10%	10%
Australia	15%	15%	10%/15%	10%/15%
Austria	10%	10%	10%	10%
Bangladesh	10%/ 15%	10%	10%	No separate provision
Belarus	10%/ 15%	10%	15%	15%
Belgium	15%	15% (10% if loan is granted by a bank)	10%	10%
Bhutan	10%	10%	10%	10%
Botswana	7.5%/ 10%	10%	10%	10%
Brazil	15%	15%	a) 25% for use of trademark; b) 15% forothers	15%
Bulgaria	15%	15%	a) 15% of royalty relating to literary, artistic, scientific works other than films or tapes used for radio or television broadcasting; b) 20%, in othercases	20%
Canada	15%/ 25%	15%	10%–15%	10%–15%
China	10%	10%	10%	10%
Columbia	5%	10%	10%	10%
Croatia	5%/ 15%	10%	10%	10%
Cyprus	10%	10%	10%	10%
Czech Republic	10%	10%	10%	10%

Country	Dividend	Interest	Royalty	FTS
Denmark	15%/ 25%	a) 10% if loan is granted bybank; b) 15% for others	20%	20%
Egypt	As per domestic law		Taxable in source country as per domestic rate	No separate provision
Estonia	10%	10%	10%	10%
Ethiopia	7.5%	10%	10%	10%
Finland	10%	10%	10%	10%
Fiji	5%	10%	10%	10%
France	10%	10%	10%	10%
Georgia	10%	10%	10%	10%
Germany	10%	10%	10%	10%
Greece	Taxable as per domestic laws in source country			No Separate provision
Hungary	10%	10%	10%	10%
Indonesia	10%	10%	10%	10%
Iceland	10%	10%	10%	10%
Ireland	10%	10%	10%	10%
Israel	10%	10%	10%	10%
Italy	15%/ 25%	15%	20%	20%
Japan	10%	10%	10%	10%
Jordan	10%	10%	20%	20%
Kazakhstan	10%	10%	10%	10%
Kenya	10%	10%	10%	10%
Korea (South)	15%	10%	10%	10%
Kuwait	10%	10%	10%	10%
Kyrgyz Republic	10%	10%	15%	15%
Latvia	10%	10%	10%	10%
Libya	Taxable as per domestic laws insource country			No separate provisions
Lithuania	5%/ 15%	10%	10%	10%

Country	Dividend	Interest	Royalty	FTS
Luxembourg	10%	10%	10%	10%
Malaysia	5%	10%	10%	10%
Malta	10%	10%	10%	10%
Mongolia	15%	15%	15%	15%
Mauritius	5%/ 15%	7.5%	15%	10%
Montenegro	5%/ 15%	10%	10%	10%
Myanmar	5%	10%	10%	No separate provision
Morocco	10%	10%	10%	10%
Mozambique	7.5%	10%	10%	No separate provision
Macedonia	10%	10%	10%	10%
Namibia	10%	10%	10%	10%
Nepal	5%/ 10%	10%	15%	No separate provision
Netherlands	10%	10%	10%	10%
New Zealand	15%	10%	10%	10%
Norway	10%	10%	10%	10%
Oman	10%/ 12.5%	10%	15%	15%
Philippines	15%/ 20%	a) 10%, if interest is received by a financial institution or insurance company; b) 15% in other cases	15% if it is payable in pursuance of any collaboration agreement approved by the Government of India	No separate provision
Poland	10%	10%	15%	15%
Portuguese Republic	10%/ 15%	10%	10%	10%
Qatar	5%/ 10%	10%	10%	10%
Romania	10%	10%	10%	10%

Country	Dividend	Interest	Royalty	FTS
Russian Federation	10%	10%	10%	10%
Saudi Arabia	5%	10%	10%	No separate provision
Serbia	5%/ 15%	10%	10%	10%
Singapore	10%/ 15%	a) 10%, if loan is granted by a bank or similar institute including an insurance company; b) 15%, in all other cases	10%	10%
Slovenia	5%/ 15%	10%	10%	10%
South Africa	10%	10%	10%	10%
Spain	15%	15%	10%	20%
Sri Lanka	7.5%	10%	10%	10%
Sudan	10%	10%	10%	10%
Sweden	10%	10%	10%	10%
Switzerland	10%	10%	10%	10%
Syria	5%/ 10%	10%	10%	No separate provision
Tajikistan	5%/ 10%	10%	10%	No separate provision
Tanzania	5%/ 10%	10%	10%	No separate provision
Thailand	10%	10%,	10%	No separate provision
Trinidad and Tobago	10%	10%	10%	10%
Turkey	15%	a) 10% if loan is granted by a bank,etc.;	15%	15%

Country	Dividend	Interest	Royalty	FTS
		b) 15% in other cases		
Turkmenistan	10%	10%	10%	10%
Uganda	10%	10%	10%	10%
Ukraine	10%/ 15%	10%	10%	10%
United Arab Emirates	10%	a) 5% if loan is granted by a bank/similar financial institute; b) 12.5%, in other cases	10%	No separate provision
United Mexican States	10%	10%	10%	10%
United Kingdom	10%/ 15%	a) 10%, if interest is paid to a bank; b) 15%, in other cases	10%/15%	10%/15%
United States	15%/ 25%	a) 10% if loan is granted by a bank/similar institute including insurance company; b) 15% for others	10%/15%	10%/15%
Uruguay	5%	10%	10%	10%
Uzbekistan	10%	10%	10%	10%
Vietnam	10%	10%	10%	10%
Zambia	5%/ 15%	10%	10%	10%

*(Indicative rates have been provided in the table above. Kindly refer respective DTAAs for better clarity)

Note: Treaty with Hong Kong is yet to be notified, Mutual agreement procedure amended with Singapore.

TDS RATE CHART[1] FOR FINANCIAL YEAR 2018–19

Section	Nature of income	When to deduct	Rate of TDS (If PAN available) (refer note 10)
192	Salary	Monthly– **at the time of payment** where estimated yearly net taxable salary exceeds tax free limit.	On the average rates on the basis of rates for individuals.
192A	Payment of accumulated balance due of Employees' Provident Fund Scheme, 1952, to Employees which is taxable in their hand (w.e.f 01-06-15)	when the amount of **payment** or aggregate amount of payment is Rs. 50,000/– or more	10%
193 (See note–1)*	**Interest on securities*** a) any debentures or securities for money issued by or on behalf of any local authority or a corporation established by a Central, State or Provincial Act; b) any debentures issued by a company where such debentures are listed on a recognised stock exchange in accordance with the Securities Contracts (Regulation) Act, 1956 (42 of 1956) and any rules made thereunder;	At the time of c**redit or payment, whichever is earlier,** when the amount exceeds Rs. 10,000/–. In case of Debentures Threshold limit is Rs. 5,000/–	10%

[1] TDS rates specified herein shall be increased by applicable surcharge and cess

Section	Nature of income	When to deduct		Rate of TDS (If PAN available) (refer note 10)
	c) any security of the Central or State Government; d) interest on any other security			
194	Dividend other than the dividend as referred to in Section 115–O	**Before making payment** to shareholder, other than dividend declared u/s 115O, when amount exceeds Rs. 2,500/–		10%
194A (See note– 2 to 5)*	Interest other than "Interest on securities"	At the time of **credit or payment, whichever is earlier,**		10%
		Interest received from banks or co – operative society engaged in banking business or post office on notified deposit	When amount exceeds Rs. 10,000	
		Interest received from others	When amount exceeds Rs. 5,000	
194B /194BB	Income by way of winnings from lotteries, crossword puzzles, card games and other games of any sort and Income by way of winnings from horse races	**At the time of payment,** **Winning from Lotteries** When exceeds Rs. 10,000 **HORSE RACE** When exceeds Rs. 10,000		30%

Section	Nature of income	When to deduct	Rate of TDS (If PAN available) (refer note 10)	
194C (See note-6)*	Payment to contractors/ sub-contractors	At the time of **credit or payment, whichever is earlier,** when the amount of a particular contract exceeds Rs. 30,000/- or the total amount of contract during the whole year exceeds Rs. 1,00,000/-	Individual / HUF	1%
			Others	2%
194D	Insurance Commission	At the time of c**redit or payment, whichever is earlier** when the amount exceeds Rs. 15,000	Resident other than Domestic company	5%
			Domestic Company	10%
194DA	Payment under life insurance policy (including Bonus)(other than amount covered u/s 10(10D)	**At the time of payment** when the amount or the total amount during the whole year is Rs. 1,00,000/- or more	1%	
194E	Payment to Non-Resident Sportsmen or Sports Association	At the time of **credit or payment, whichever is earlier**	20%	
194EE	Payment in respect of deposit under National Savings scheme (NSS)	**At the time of payment**, when the amount is Rs. 2500/- or more	10%	
194F	Payment on account of repurchase of unit by Mutual Fund or Unit Trust of India	**At the time of payment**	20%	
194G	Commission on sale of lottery tickets	At the time of **credit or payment, whichever is earlier** when the amount exceeds Rs. 15,000	5%	

Section	Nature of income	When to deduct	Rate of TDS (If PAN available) (refer note 10)	
194H	TDS on commission/brokerage	At the time of **credit or payment, whichever is earlier** when the amount exceeds Rs. 15,000	5%	
194I (See note-7)	Rent	At the time of **credit or payment, whichever is earlier,** when the amount exceeds Rs. 1,80,000/-	If rent is for land, building or furniture	10%
			If the rent is for plant or Machinery, Equipment	2%
194IA (See note-8)	Payment on transfer of certain immovable property other than agriculture land.	At the time of **credit or payment, whichever is earlier,** when consideration for transfer is Rs. 50 lacs or more	1%	
194IB	Rent payable by an individual or HUF not covered u/s. 194I (W.E.F. from 01.06.2017)	Tax shall be deducted on such income at the time of credit of rent, for the last month of the previous year or the last month of tenancy if the property is vacated during the year, as the case may be, to the account of the payee or at the time of payment, whichever is earlier when payment exceeds Rs. 50,000 p.m.	5%	
194IC	Payment of Consideration (not being in kind) under Joint Development Agreement or other similar agreement	At the time of **credit or payment, whichever is earlier**	10% (Applicable from 01.04.2017)	
194J	**Any sum paid by way of** a) Fee for professional services,	At the time of **credit or payment, whichever is earlier,** when the amount exceeds	10%	

Section	Nature of income	When to deduct	Rate of TDS (If PAN available) (refer note 10)	
	b) Fee for technical services c) Royalty, d) Remuneration / fee / commission to a director or e) For not carrying out any activity in relation to any business f) For not sharing any know-how, patent, copyright etc.	Rs. 30,000/- **No limit for Director's Fees.**	in case of payee, being a person engaged only in the business of operation of call centre (w.e.f. 01.06.2017)	2%
194LA	Payment on transfer of certain immovable property other than agricultural land (i.e. payment of compensation on compulsory acquisition) (Read Note- 9)	**At the time of payment** if amount exceeds Rs. 2,50,000	10%	
194LB	Payment of interest on infrastructure debt fund to non-resident or foreign company	At the time of **credit or payment whichever is earlier**	5%	
194LBA	Income from units of a business trustbeing a special purpose vehicle to Residents (applicable from 01.10.2014)	At the time of **credit or payment whichever is earlier**	Resident	10%
			Non-resident	5%
	Certain income from units of real estate investment trust (applicable from 01.10.2014)		Resident	10%
			Non-resident	At the rates in force or at the rates

Section	Nature of income	When to deduct	Rate of TDS (If PAN available) (refer note 10)	
				specified in DTAAs whichever is beneficial
194LBB	Investment fund paying an income to a unit holder [other than income which is exempt under Section 10(23FBB)] shall deduct tax there from	At the time of **credit or payment, whichever is earlier**	Resident	10%
			Non-residents	At the rates in force or at the rates specified in DTAAs whichever is beneficial
194LBC	Income in respect of investment in securitisation trust. (From 01.06.2016)	At the time of **credit or payment whichever is earlier**	Resident individual or HUFs	25%
			Other Residents	30%
			Non-residents	At the rates in force or at the rates specified in DTAAs whichever is beneficial
194LC	Payment of interest by an Indian Company or a business trust in respect of money borrowed in foreign currency under a loan agreement or by way	At the time of **credit or payment, whichever is earlier**	5%	

Section	Nature of income	When to deduct	Rate of TDS (If PAN available) (refer note 10)
	of issue of long-term bonds (including long-term infrastructure bond) And in respect of monies borrowed by it from a source outside India by way of issue of rupee denominated bond before the 1st day of July, 2020		
194LD	Payment of interest on rupee denominated bond of an Indian Company or Government securities to a Foreign Institutional Investor or a Qualified Foreign Investor (specified withholding tax on interest payment under section 194LD will now be available on interest payable before the 1st July, 2020)	At the time of **credit or payment whichever is earlier**	5%

Notes:

1. Securities includes listed as well as unlisted debentures issued by companies in which public are substantially interested.

2. In case of interest payment on time deposits by co-operative banks to its members the TDS Provision is applicable from 1-6-2015.

3. TDS provisions under Section 194A shall not apply to income paid by way of interest on the compensation amount awarded by the Motor Accidents Claims

Tribunal where the amount of such income does not exceed Rs. 50,000/- and further TDS on interest payment on compensation amount awarded by Motor Accident Claim Tribunal is deductible at the time of payment instead of accrual (w.e.f. 01.06.2015). No TDS applicable on interest paid on partner's capital.

4. As per amended definition of 'time deposits' under section 194(3) it now includes recurring deposits also. This implies that now, interest on recurring deposits is also subject to TDS.

5. Bank wise Income to be considered for TDS deduction on time deposits instead of Branch-

6. **From 01.06.2015 –**

- **From 01.06.2015** - If the payment is made to contractor/sub-contractor in transport business, no TDS shall be deducted at source in the course of payment for plying, hiring or leasing goods carriages if the contractor provides PAN Number and such contractor owns ten or less goods carriage at any time during the previous year and furnishes a declaration to that effect. (w.e.f. 01.06.2015)

- **Up to 31.05.2015**– No deduction shall be made from any sum credited or paid or likely to be credited or paid during the previous year to the account of a contractor during the course of business of plying, hiring or leasing goods carriages on furnishing of his Permanent Account Number, to the person paying or crediting such sum.

7. No TDS deduction shall be made under section 194-I of the Act where the income by way of rent is credited or paid to a business trust, being a real estate investment trust (REIT), in respect of any real estate asset held directly by such REIT. (w.e.f. 01-04-2015)

8. In case of section 194IA, the sub-registrar shall register the document only after the challan for payment of TDS is presented before him.

9. Section 194LA has been amended to provide that no deduction shall be made under this section where such payment is made in respect of any award or agreement which has been exempted from levy of income-tax under section 96 (except those made under section 46) of Right to Fair Compensation and Transparency in Land Acquisition, Rehabilitation and Resettlement Act (RFCTLARR Act). This amendment will take effect from 1st April, 2017.

10. In case, the payee is not able to furnish PAN to the payer, tax shall be deducted at the higher of the following rates:

    (i) rate specified in the relevant provision in the IT Act,

    (ii) at the rates specified in force

    (iii) at the rate of 20%

Abbreviations

Terms	Definition
API	Active Pharmaceutical Ingredients
ANDA	Abbreviated New Drug Application
CDSCO	Central Drugs Standard Control Organization
CAPA	Corrective And Preventive Actions
D & C Act	Drugs and Cosmetics Act, 1940
DCGI	Drugs Controller General of India
EMEA	European Medicines Agency
FDA	The Food and Drug Administration
GMP	Good Manufacturing Practices
GCP	Good Clinical Practices
GDPR	General Data Protection Regulation
GDocP	Good Documentation Practices
HSA	Health Sciences Authority
IND	Investigational New Drug
ICH	The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICMR	Indian Council for Medical Research
ICRS	International Chemical Reference Substances
MHRA	Medicines and Healthcare products Regulatory Agency
NPPA	National Pharmaceutical Pricing Authority
NAFDAC	The National agency for Food Administration and Control
NDA	New Drug Application
OECD	The Organisation for Economic Co-operation and Development
OTC	Over-the-counter
PMA	Premarket Approval Application
QRM	Quantitative Risk Management
SOP	Standard Operating Procedures
SAE	Serious Adverse Event
TGA	Therapeutic Goods Administration
TPO	Transfer Pricing Officer
US FDA	United states Food and Drug Administration
WTO	World Trade Organization

Notes

Notes

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Mumbai – 400 093

201, Shree Padmini
Teli Galli Junction
Andheri (E), Mumbai – 400 069

New Delhi – NCR
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Noida – 201 301

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Chennai – 600 028

1A, Chamiers Apartments
62/121, Chamiers Road
R. A. Puram, Chennai – 600 028

Kolkata
A-6, 12th Floor
Chatterjee International Centre
33A, Jawaharlal Nehru Road
Kolkata – 700 071

Bengaluru
3rd Floor, B Wing
Jubilee Building, 45, Museum
Road, Bengaluru – 560 025

Surat
DTA-2, G-02 to G-05 Plot
Gujarat Hira Bourse
Ichhapore-2
Surat – 394 510

T-720, Belgium Tower
Opp. Linear Bus Stop
Ring Road, Surat – 395 002

B/604-605, Tirupati Plaza
Athwa Gate, Nanpura
Surat – 395 001

Hyderabad
217, Maruthi Corporate Point
Swapnalok Complex
92, Sarojini Devi Road
Secunderabad – 500 003

Ahmedabad
B-504, Narnarayan Complex
Navrangpura
Ahmedabad – 380 009

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