India Regulatory Updates

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BACKGROUND

- Drugs fall under **concurrent list** of constitution of India
- Federal structure, enforced by both, central and provincial agencies
  - **Central-CDSCO**
  - **State/UT** Drug Control Authorities (28 STATES + 8 UT DCAs)
- Drugs and Cosmetics Act, 1940
    - Drugs Rules, 1945
    - Medical Devices Rules, 2017
    - New Drugs And Clinical Trial Rules, 2019
    - Cosmetics Rules, 2020
- **Import, Manufacture, Sale and Distribution** of Drugs, Cosmetics, Medical Devices, Vaccines, Veterinary medicines, AYUSH drugs, blood and blood products etc.
- Export, through various guidelines and administrative orders

MANDATES

- **Quality, Safety** and **Efficacy** by CDSCO and State/UT DCAs
- **Prices** are regulated by NPPA (availability and affordability)
- **Patents/IPR** is regulated By DPIIT
- Promotion of **Research** is regulated By ICMR, DBT, DST etc.
- Promotion of pharma industry-incentives or **schemes** By DOP
- **Export** is regulated by DGFT
- **Advertisements-** DMR(OA) ACT, 1954)
- **Narcotics and Psychotropic** Substances Act, 1980 by NCB/MHA
- **Traditional medicines**-AYUSH
- CPCSEA- Prevention to cruelty on **Animals** during Trials
- RCGM- **Mutagenicity** of r-DNA products (Drugs/Food etc.)
- GEAC-Environmental clearance for use of **Hazardous micro-organisms**

CONTROL OVER QUALITY (END-TO-END)

- Test licences (Research and Development, for Import and Mfg.)
- Registration of CROs and BABE study centres
- Permissions for conducting Clinical Trial/BABE studies (Clinical Research)
- Import Registration and Import Permissions (Imported drugs)
- Manufacturing licences (SLAs, Joint inspections by CDSCO)
- Sale and distribution licences -SLAs
- Sale premises (Retail, including supply chain CNF / Wholesalers) -SLAs
- Sampling by drugs inspectors (Imported/in-country mfg. drugs)
- Testing at Govt. Laboratories (Central and State/UT Drug Testing Labs)
- Investigations and Raids

CONTROL OVER QUALITY (END-TO-END)

- Alerts on NSQs
- Recall mechanism
- Prosecutions
- Regulatory and administrative actions
- Pharmacovigilance, Materiovigilance, Heamovigilance mechanism
- Lifecycle management (Label change, Listing in schedule G, H, H1, X, restriction, prohibitions, discontinuation, banning etc.)
- Unique provisions for compensation mechanism in cases of SAE, Injury or Death related to Clinical Trials or Clinical Investigations
- Medical management and post trial access

Salient features of Proposed Schedule M:-

GMP requirements upgraded in line with WHO norms vide G.S.R. 922 (E) dated 28.12.2023).

- The proposed Schedule M prescribes the following major additional features in addition to the existing Schedule M
  - Pharmaceutical Quality System (PQS)
  - Quality Risk Management (QRM)
  - Product Quality Review (PQR)
  - Qualification and Validation
  - Establishment of system to recall the defective products
  - Change control
  - Self inspection team & Quality audit
  - Suppliers audit and approval
  - Stability studies
  - Validation of GMP related computerized system
  - Specific Requirements for Manufacturing of Hazardous products, Biological Products, Radiopharmaceutical and Phytopharmaceuticals.

Schedule M (Good Manufacturing Practices and Requirements of Premises, Plant and Equipment for Pharmaceutical Products)

- Various workshops were also conducted across the country for awareness of the stakeholders.
- RPTUAS Scheme
- The central Government has provided time for implementation of the revised Schedule M as mentioned below:

Category of manufacturers	**Time line for implementation**
Large manufacturers (Turnover> 250 crores)	Six month from the date of publication of these rules. (i.e. 28/06/2024)
Small and Medium manufacturers (Turnover≤ 250 crores)	Twelve months from the date of publication of these rules. (i.e. 28/06/2024)

UPDATES ON DRUGS RULES, 1945

- Bioequivalence and Stability Study is made mandatory for grant of manufacturing licence (G.S.R. 327 (E) dated 03.04.2017).
- Joint inspections with state licensing authorities for grant of licence and periodic inspections (G.S.R. 1337(E) dated 27.10.2017).
- Marketers are also made responsible for ensuring quality of the pharmaceutical products marketed by them around the world [G.S.R. 101(E), dated 11.02.2020]
- QR code/Bar code on all APIs and top 300 brands of formulations (GSR 20 (E) dated 18.01.2022 and GSR 567 (E) dated 13.08.2019)

SALIENT FEATURES OF MEDICAL DEVICE RULES, 2017

- In harmonization with GHTF/IMDRF (GSR 78 (E) dated 31.01.2017)
- Risk based classification (Class A, B, C, D)
- Provisions of notified bodies
- Quality management system in line with ISO 13485
- Provisions related to the 'essentials principles of safety and performance' for manufacturers have been specified in the rules;
- Separate provisions for regulation of clinical investigations of Investigational Medical Devices (i.e. new devices)
- Provision to designate or establish Medical Device Testing Laboratories to verify conformance with the quality standards.
- Provisions enabled for fast track approval for diagnostics.
- Compensation related to Injury/death
- All devices intended for use in human beings or animals are notified with the definition of medical devices (S.O. 648(E) dated 11.02.2020)
- All medical devices are brought under regulation in phase wise manner vide G.S.R 102(E) dated 11.02.2020

SALIENT FEATURES OF MEDICAL DEVICE RULES, 2017

Risk Based Class	Voluntary Registration	Mandatory Registration	Licensing Regime
Class A & B	01.04.2020 to 30.09.2021 (18 months)	01.10.2021 to 30.09.2022 (12 months)	w.e.f. 01.10.2022
Class C & D	01.04.2020 to 30.09.2021 (18 months)	01.10.2021 to 30.09.2023 (24 months)	w.e.f. 01.10.2023

Phase wise manner of licensing in Medical Devices

UPDATES ON NEW DRUGS AND CLINICAL TRIALS RULES, 2019

(Before 19.03.2019, new drugs and clinical trials were regulated under PART X-A of the Drugs Rules,1945 and Schedule-Y to the rules)

- NDCT Rules, 2019, effective from 19.03.2019
- New Drugs definition scope has been broadened to include-
  - Phytopharmaceuticals
  - Living modified organism,
  - Monoclonal anti-body,
  - Stem cell derived product,
  - Gene therapeutic product or
  - Xenografts
- Waiver to academic clinical trials
- Various provisions for promoting scientific and ethical clinical research as well as development and approval of new drugs.

NEW DRUGS AND CLINICAL TRIALS RULES

- Provisions of accelerated /expedited approval to a new drug for a disease or condition, taking into account
  - ❖ Severity, rarity, or prevalence and
  - ❖ availability or lack of alternative treatments
  - ❖ Provided that there is a prima facie case of the product being of meaningful therapeutic benefit over the existing treatment.
- Provisions for pre-consultation have been incorporated (pre-submission and post submission meetings)
- Compensation related to SAE/death
- Separate provisions for registration of Ethics Committee for BA/BE study and Biomedical health Research
- Draft has been published for registration of CRO for comments from stakeholders vide GSR 364(E) dated 11.05.2023

NEW DRUGS AND CLINICAL TRIALS RULES

- Pre-defined timelines.

Type of Application	Timelines
CT (innovated in India):	within 30 days
CT (if drug is already approved by other country):	within 90 days
New drug	within 90 days
Processing of Import License	90 days
If the central licensing authority does not communicate, the “permission to conduct the clinical trial shall be deemed to have been granted”.	

Recent initiatives to strengthen the regulatory system

- Digital intervention for monitoring & fixing accountability:
  - ❖ SUGAM Online, for Drugs, Cosmetics, Vaccines, Blood products etc.
  - ❖ SUGAM Online, for Medical devices
  - ❖ SUGAM Lab Testing, for labs
  - ❖ ONDLS-Online National Drug Licensing System
- NSWS Portal developed by DPIIT
- New modules developed under SUGAM portal
  - Submission of PSURs
  - Post Approval Changes for Vaccines
  - Manufacturing license for Vaccines
  - Blood centre and components licensing

- Capacity Building:
  - ❖ 1837+ current strength of CDSCO (Regulatory and Quality control staff)
  - ❖ Cadre expansion for Drugs and Medical Devices verticals.
  - ❖ Dedicated Training Academy at NIHFW
  - ❖ Online seminars, symposiums and trainings
  - ❖ Various National and International collaborative capacity building programs

Regulatory Measures

- Risk Based Inspections have been initiated in order to assess the regulatory compliance.
- PV audits
  - Online filing of PSUR through SUGAM portal
- Issue of NoC for export of Unapproved New Drugs/New drugs by CDSCO
  - Streamlining the application processing procedure
- NAP AMR 2.0
  - Dedicated consultations with the States
  - Monitoring of waste disposal of Antimicrobials during Inspections
  - Dedicated Nodal Cell at each State
  - Sharing of best practices
  - Sensitising the manufacturers and Chemsists
- Ayush vertical at CDSCO
- National Drug Data base
  - 9,461 Firms
  - 759367 drug formulations out of which 178102 brand names

Recent initiatives to strengthen the regulatory system

- Skills and Competency building trainings and workshops:
  - ❖ Risk based inspections of Drugs manufacturing facilities
  - ❖ Investigation techniques and launching of prosecutions
  - ❖ Refresher course on New Drugs and Clinical Trials Rules 2019
  - ❖ NRA Assessment of Vaccines*
  - ❖ Clinical & CMC evaluation of New Drugs, Vaccine and Recombinant products. Biostatistics
  - ❖ Role of International Organizations viz. WHO, ICH, PIC/s/ICDRA/ ICMRA/IMDRA/MSM and Emergency Preparedness
  - ❖ Implementation of QMS in Medical Device
  - ❖ Regenerative Medicine and Gene therapy
  - ❖ GMP of Oral Solid Dosage and Topical formulation
  - ❖ Clinical Trials

Recent initiatives to strengthen the regulatory system

- Draft of Drugs, Medical Devices and Cosmetics Bill, 2023
- Revision of GMP principles (Scheduled M) in line with WHO- TRS requirements to include comprehensive provisions for PQS, QRM, PQR, validations, computerized data archival etc.
- Risk Based Inspections :
  - ✓ Phase wise RBI of manufacturing facilities, 301 such RBI conducted across country.
  - ✓ Phase wise RBI of testing facilities, 126 such RBI conducted across country.
  - ✓ Non compliance to applicable provisions were strictly dealt,
- Monthly review meetings with State Regulators.
- Regular meetings with industry associations.
- Quality Testing of Cough Syrup for export
  - ✓ Indian Pharma monographs, revised with stringent limits of EG/DEG in PEG and Glycerin
  - ✓ Every consignment of Cough syrup to be tested at Govt. labs before its export
  - ✓ Approximately 4168 samples has been tested till now.

Recent initiatives to strengthen the regulatory system

Drugs, Medical Devices and Cosmetics Bill, 2023

- MoHFW published the draft Bill seeking suggestions/ objections from the public stakeholders.
- The purpose of the Bill is to consolidate the law relating to the import, manufacture, distribution and sale of drugs, medical devices and cosmetics.
- The objectives of the Bill is to –
  - ensure the quality, safety, efficacy, performance and clinical trial of new drugs,
  - clinical investigation of investigational medical devices and
  - clinical performance evaluation of new in vitro diagnostic medical devices,
  - for encouraging innovation in development,
  - protection and promotion of health, and
  - for matters connected therewith or incidental thereto
- The Ministry held consultation with the industry Associations on issues of concern

Ease of Doing Business

In order to improve transparency, accountability and fast tracking the approval:

- E-governance through **SUGAM Portal**,
- Establishment of **Public Relation Office** at all offices of CDSCO,
- Video Conferencing facility for **Start Ups**, **Innovators, etc.**
- Providing **prompt and predictable** services to the stakeholders,
- **Streamlining** of regulatory process with global pharma. ecosystem
- **Accelerating** the regulatory approvals by **regulatory reliance**

India 2024

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19TH INTERNATIONAL CONFERENCE OF DRUG REGULATORY AUTHORITIES

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19th International Conference of Drug Regulatory Authorities

New Delhi, India | 14th October - 18th October 2024

INTERNATIONAL COLLABORATION

Sr. No.	Country Name	Drug Regulatory Agency	MoU/MoC/MoI
1	United States America	US Food and Drugs Administration	MoU
2	United Kingdom	The United Kingdome Medicines and Healthcare Products Regulatory Agency	MoU
3	Sweden	The Swedish Medical Products Agency (MPA)	MoI
4	Japan	The Ministry of Health, Labour and Welfare of Japan	MoC
5	Brazil	ANVISA	MoU
6	Argentine	The National Administration of Drugs, Food & Medical Devices	MoU
7	Saudi Arabia	Saudi Food and Drug Authority	MoU
8	Afghanistan	The National Medicines and Healthcare products regulatory authority	MoU
9	Germany	Drugs Regulatory Authority, Germany	MoU
10	Suriname	Medicines Regulatory Authority, Ministry of Health	MoU
11	Dominican Republic	Directorate General for Medicines, Foods and Sanitary Products	MoU
12	Ecuador	ARCSA	MoU
13	Russia	Federal Service on Surveillance in Healthcare & Social Development(Russian Federation)	MoU
14	The Netherlands	THE MINISTRY OF HEALTH, WELFARE AND SPORT, KINGDOM OF THE NETHERLANDS On behalf of MEB, IGJ, CCMO	MoU
15	BRICS	BRICS Drugs regulatory authorities	MoU
16	Denmark	DKMA	JDI

NOTE: More than 30 MoUs are under negotiations & MoU with Chile, Peru is ready for signing.


Thank You !!