REGULATORY AFFAIRS

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Syllabus

Regulatory affairs:

Introduction, Historical overview of Regulatory Affairs, Regulatory authorities, Role of Regulatory Affairs department, Responsibility of Regulatory Affairs Professionals

Regulatory requirements for drug approval:

Drug Development Teams, Non-Clinical Drug Development, Pharmacology, Drug Metabolism and Toxicology, General considerations of Investigational New Drug (IND) Application, Investigator's Brochure (IB) and New Drug Application (NDA), Clinical research / BE studies, Clinical Research Protocols, Biostatistics in Pharmaceutical Product Development, Data Presentation for FDA Submissions, Management of Clinical Studies.

Introduction

- Regulatory Affairs (RA), also called Government Affairs, is a profession developed from the desire of governments to protect public health by controlling the safety and efficacy of products in areas including pharmaceuticals, veterinary medicines, medical devices, pesticides, agrochemicals, foods, cosmetics and complementary medicines etc.
- As a discipline, regulatory affairs cover a broad range of specific skills and occupations.
- Under the best of circumstances, it is composed of a group of people who act as a liaison between the government, industry, and consumers to ensure that marketed products are safe and effective when used as it advertised.

- People who work in regulatory affairs negotiate the interaction between the regulators (the government), the regulated (industry), and the market (consumers) to get good products to the market and to keep them there while preventing bad products from being sold.
- Pharmaceutical Drug Regulatory Affairs (DRA) is a dynamic field that includes scientific, legal and commercial aspect of drug-development.
- Drug development to commercialization is highly regulated.
- Every drug before getting market approval must undergo rigorous scrutiny and clinical trials to ensure its safety, efficacy and quality.
- These standards are set by regulatory authorities of their respective countries such as FDA in US and CDSCO in India etc.

Regulation of Drug products involve following areas:

- Non-clinical and Clinical Drug Development Guidelines
- Licensing (Patent)
- Drug Registration
- Manufacturing
- Quality and safety Guidance
- Pricing and Trademark
- Marketing, Import and Distribution of Drug products
- Pharmacovigilance (Adverse Drug Reactions monitoring)

Historical overview of Regulatory Affairs

Year	Event	Purpose
1902	Biologics Control Act (Diphtheria Epidemic)	To regulate the sale of viruses, serums, toxins and analogous products
1906	Pure Food and Drug Act	Prevent false claims
1930	FDA takes it current name	Agency is purely regulatory – no research functions
1938	Federal Food, Drug, and Cosmetic Act	Require proof of safety before marketing
1949	First publication of FDA " Guidance to Industry"	Address the appraisal of toxic chemicals in foods
1962	Kefauver – Harris Drug Amendments (Thalidomide tragedy)	Require proof of efficacy and safety before marketing
1976	Medical Device Amendments	Risk based classification system for all medical devices intended for human use

Year	Event	Purpose
1987	Prescription Drug Marketing Act	Ensure that pharmaceutical products purchased by consumers are safe and effective, and free from counterfeit, adulterated, misbranded, subpotent, or expired drugs.
2004	Pharmaceutical cGMPs for the 21st Century – A Risk Based Approach	Emphasize risk-based approaches to development and manufacturing
2004	PAT – A Framework for Innovative Pharmaceutical Development, Manufacturing and Quality Assurance	Achieve greater understanding of drug development and manufacturing processes. Data acquisition and multivariate analysis cited as important tools
2005	ICH Harmonized Tripartite Guideline: Pharmaceutical Development, Q8	Foster quality by design and the understanding of design space emphasis on design of experiments to define interactions and work in multidimensions

Year	Event	Purpose
2005	ICH Harmonized Tripartite Guideline: Quality Risk Management, Q9	Encourage the use of quality risk – management tools in all phases of a product's lifecycle
2007	ICH Harmonized Tripartite Guideline: Pharmaceutical Quality System, Q9	Enhance science and risk-based regulatory approaches

Regulatory Authorities in the World

Country	Regulatory Authority
India	• Central Drugs Standard Control Organization (CDSCO) • Drugs Controller General of India (DCGI)
USA	Food and Drug Administration Act (USFDA)
UK	Medicines and Health Care products Regulatory Agency (MHRA)
Australia	Therapeutic Goods Administration (TGA)
Japan	• Japanese Ministry of Health, Labour, and Welfare (MHLW) • Pharmaceuticals and Medical Devices Agency (PMDA)
Canada	Health Canada
Brazil	Agency Nacional degradation Vigilancia Sanitaria (ANVISA)
South Africa	Medicines Control Council (MCC)
Europe	• European Directorate for Quality Medicines (EDQM) • European Medicines Evaluation Agencies (EMEA)

- It was observed that regulatory guidelines differ with respect to territorial requirements; this demanded the need for universal harmonization.
- Thus, The International Council for Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) was founded in 1990 by united efforts of the United States, Europe and Japan to bring together different regulatory bodies globally and set ICH Guidelines for pharmaceutical drug product development.
- Since its inception, the ICH has evolved gradually with a mission to attain better harmonization towards development and registration of medicines with a higher degree of safety, efficacy and quality worldwide.
- Although ICH has harmonized the drug regulatory aspects worldwide, the regional regulatory bodies continue to play a pivotal role in drug approvals across the territory.

Role of Regulatory Affairs Department

In Development phase

- Ensuring that the legislative requirements are met
- Recruit Scientific Advice – authorities
  – Advice on development studies to demonstrate safety, quality and efficacy parameters.
- Set up regulatory strategy.
- Participate in cross-functional project teams.
- Ensure the application of guidelines for clinical trials.
- Submission of application to conduct clinical trials.
- Managing the regulatory submission –
  – Minimize time to market (every day counts!)
  – Advice on a global development plan

- Optimize submission strategies –
  – Dossier preparation
  – Format, document re-uses
  – Electronic submissions
  – Review high-level documents/reports
- Interact with the commercial side of business such as pricing and reimbursement.

In approval phase

- Check the progress of evaluation and anticipate questions.
- Clarify raised questions, and plan response and strategies with other departments.
- Plan and manage agency meetings/hearings.
- Negotiate approval and Product Information with agencies.

In post-approval phase

- Compliance
- Submission of variations/amendments
- Renewals
- Pharmacovigilance
- Product information review
- New indications / new formulations
- Regulatory input to development plans/ Regulatory Intelligence.

- Keep in touch with international legislation, guidelines and customer practices
- Keep up to date with a company's product range
- Ensure that a company's products comply with the current regulations.
- The Regulatory Affairs professional's job is to keep track of the ever-changing legislation in all the regions in which the company wishes to distribute its products.
- They also advise on the legal and scientific restraints and requirements, and collect, collate, and evaluate the scientific data that their research and development colleagues generate.
- Formulate a regulatory strategy for all appropriate regulatory submissions for domestic, international and/or contract projects.

- Coordinate, prepare and review all appropriate documents for example dossier and submit them to regulatory authorities within a specified time frame in conjugation with the organization.
- Prepare and review of SOPs related to RA. Review of BMR, MFR, change control and other relevant documents.
- Monitor the progress of all registration submissions.
- Maintain approved applications and the record of registration fees paid against submission of DMF’s and other documents.
- Respond to queries as they arise, and ensure that registration/ approval is granted without delay.
- Impart training to R&D, Pilot plant, ADI and RA. Team members on current regulatory requirements.

- Advising their companies on the regulatory aspects and climate that would affect proposed activities. I.e. describing the “regulatory climate” around issues such as the promotion of prescription drugs and Sarbanes-Oxley compliance.
- Manage review audit reports and compliance, regulatory and customer inspections.
- Regulatory Affairs professionals help the company avoid problems caused by badly kept records, inappropriate scientific thinking or poor presentation of data. In most product areas where regulatory requirements are imposed, restrictions are also placed upon the claims which can be made for the product on labelling or in advertising.
- Have a duty to provide physicians and other healthcare professionals with accurate and complete information about the quality, safety and effectiveness of the product.

Responsibility of Regulatory Affairs Professionals

- Ensuring that their companies comply with all of the regulations and laws pertaining to their business.
- Working with federal, state and local regulatory agencies and personnel on specific issues related to their business.
- Advising companies on the regulatory aspects and climate that would affect their proposed activities.
- Keep in touch with international legislation, guidelines and customer practices.
- Keep up to the date with a company's product range.
- Collect, collate, and evaluate the scientific data that their research and development colleagues are generating.

Responsibility of Regulatory Affairs Professionals

- Formulate regulatory strategies for all appropriate regulatory submissions such as domestic, international and/or contract projects.
- Coordinate, prepare and review all appropriate documents for example dossier and submit them to regulatory authorities within a specified time frame in conjugation with the organization.
- Prepare and review of SOPs related to RA. Review of BMR, MFR, change control and other relevant documents.
- Monitor the progress of all registration submission.
- Maintain approved applications and the record of registration fees paid against submission of DMF's and other documents.
- Respond to queries and ensure that registration/ approval are granted without delay.

Responsibility of Regulatory Affairs Professionals

- Participate in R&D training, Pilot plant Scale Up, and Post Marketing Surveillance (ADR).
- Manage and review audit reports and compliance, regulatory and customer inspections.
- Provide accurate and complete information about the quality, safety and effectiveness of the product to the physicians and other healthcare professionals.