# Research Regulations US


Module 5 Topic 2

# United States

The Food and Drug Administration is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation.

# Structure of USFDA

- The Food and Drug Administration (FDA) is an agency within the U.S. Department of Health and Human Services
- It consists of the Office of the Commissioner and four directorates overseeing the core functions of the agency:
  - Medical Products and Tobacco
  - Foods and Veterinary Medicine
  - Global Regulatory Operations and Policy
  - Operations

# Organization

Commissioner FDA

- Biologics
- Drugs
- Devices
- Foods
- Veterinary
- Tobacco
- Oncology
- Regulatory Affairs

# Responsibilities of USFDA

- Protection of the public health by assuring that foods (except for meat from livestock, poultry and some egg products which are regulated by the U.S. Department of Agriculture) are safe, wholesome, sanitary and properly labeled
- Ensuring that human and veterinary drugs, and vaccines and other biological products and medical devices intended for human use are safe and effective

# Code of Federal Regulation

- The Code of Federal Regulations (CFR) is a codification of the general and permanent rules published in the Federal Register by the Executive departments and agencies of the Federal Government
- Title 21 of the CFR is reserved for rules of the Food and Drug Administration.
- CFR 21 was received from the Government Printing Office (GPO) and contains the most recently received revision.
- Food and Drugs: Parts 1 to 1499 different types of parts to food, drug , cosmetic and medical devices and etc.

# Code of Federal Regulation
# Parts of 21 CFR

- 21 CFR part 11- Electronic submission and Electronic signature
- 21 CFR part 50- Protection of human subjects
- 21 CFR part 54- Financial Disclosure by Clinical Investigators
- 21 CFR part 56- Institutional Review Board
- 21 CFR part 101-Food Labelling
- 21 CFR part 104-Nutritional quality guidelines for foods
- 21 CFR part 106- Infant Formula Quality Control Procedures

# Approval process for a new drug

- Drug companies seeking FDA approval to sell a new prescription drug in the United States must test it in various ways
- First are laboratory and animal tests
- Next are tests in humans to see if the drug is safe and effective when used to treat or diagnose a disease
- After testing the drug, the company then sends FDA an application called a New Drug Application (NDA)
- Some drugs are made out of biologic materials. Instead of an NDA, new biologic drugs are approved using a Biologics License Application (BLA)

# FDA Drug Review

- If a drug developer has evidence from its early tests and preclinical and clinical research that a drug is safe and effective for its intended use, the company can file an application to market the drug
- The FDA review team thoroughly examines all submitted data on the drug and makes a decision to approve or not to approve it

# New Drug Application

- A New Drug Application (NDA) tells the full story of a drug. Its purpose is to demonstrate that a drug is safe and effective for its intended use in the population studied
- A drug developer must include everything about a drug - from preclinical data to Phase 3 trial data - in an NDA. Developers must include reports on all studies, data, and analyses. Along with clinical results, developers must include:
- Proposed labeling
- Safety updates
- Drug abuse information

# New Drug Application (contd)

- Patent information
- Any data from studies that may have been conducted outside the United States
- Institutional review board compliance information
- Directions for use

# New Drug Application Approval

- In cases where FDA determines that a drug has been shown to be safe and effective for its intended use, it is then necessary to work with the applicant to develop and refine prescribing information
- This is referred to as “labeling.” Labeling accurately and objectively describes the basis for approval and how best to use the drug

# European Medicines Agency (EMA)

- The EMA is a **decentralized agency** of the European Union (EU) responsible for the **scientific evaluation, supervision** and **safety monitoring** of medicines in the EU.

# Mission

Protect human and animal health

- Facilitate development and access to medicines
- Evaluate application for marketing authorization
- Monitor safety of medicines across their life cycle
- Provide reliable information on human and veterinary medicines in lay language

# The European Union


Total 31 members of European Union

# Structure of EMA

- EMA is governed by an **independent Management Board**. Its day-to-day operations are carried out by the EMA staff, based in London, overseen by EMA's Executive Director

- EMA is a **networking organization** whose activities involve thousands of experts from across Europe. These experts carry out the work of EMA's scientific committees

# Structure of EMA (contd)

**Management Board**

- The Management Board consists of **36 members**, appointed to act in the public interest, who do not represent any government, organization or sector
- The Board sets the Agency's budget, approves the annual work programme and is responsible for ensuring that the Agency works effectively and co-operates successfully with partner organizations across the EU and beyond

# Structure of EMA (contd)

**Scientific Committees**

- Committee for Medicinal Products for Human Use (CHMP)
- Pharmacovigilance Risk Assessment Committee (PRAC)
- Committee for Medicinal Products for Veterinary Use (CVMP)
- Committee for Orphan Medicinal Products (COMP)
- Committee on Herbal Medicinal Products (HMPC)
- Committee for Advanced Therapies (CAT)
- Paediatric Committee (PDCO)

# Structure of EMA (contd)

- The committees and working parties also contribute to the **development of medicines** and medicine regulation, by:
  - Providing scientific advice to companies researching and developing new medicines
  - Preparing scientific guidelines and regulatory guidance to help pharmaceutical companies prepare marketing authorisation applications
  - Contributing to the harmonisation of regulatory requirements n the EU and internationally

# Committee for Medicinal Products for Human Use (CHMP)

- **Role of the CHMP**
- The CHMP plays a vital role in the authorization of medicines in the European Union (EU).

# Pharmacovigilance Risk Assessment Committee (PRAC)

**Role of the PRAC**

- The PRAC is responsible for assessing all aspects of **risk management** of human medicines, including:
  - The detection, assessment, minimization and communication of the risk of adverse reactions, while taking the therapeutic effect of the medicine into account
  - Design and evaluation of post-authorisation safety studies
  - Pharmacovigilance audit

# Committee for Orphan Medicinal Products (COMP)

**Role of COMP**

- The committee responsible for recommending orphan designation of medicines for rare diseases.
- The COMP also advises and assists the European Commission on matters related to orphan medicines, including:
  - Developing and establishing an EU-wide policy
  - Drawing up detailed guidelines
  - Liaising internationally

# Committee on Herbal Medicinal Products (HMPC)

**Role of HMPC**

- The committee responsible for compiling and assessing scientific data on herbal substances, preparations and combinations, to support the harmonization of the European market.

# Committee for Advanced Therapies (CAT)

**Role of CAT**

- The committee responsible for committee responsible for assessing the quality, safety and efficacy of advanced therapy medicinal products (ATMPs) and scientific developments in the field.
  - The committee's main responsibility is to prepare a draft opinion on each ATMP application submitted to EMA, before the Committee for Medicinal Products for Human Use (CHMP) adopts a final opinion on the marketing authorization of the medicine concerned.

# Paediatric Committee (PDCO)

**Role of PDCO**

- The scientific committee responsible for activities on medicines for children and to support the development of such medicines in the EU by providing scientific expertise and defining paediatric needs.
  - The PDCO's main role is to assess the content of paediatric investigation plans (PIPs), which determine the studies that companies must carry out in children when developing a medicine. This includes assessing applications for a full or partial waiver and for deferrals.

# Authorisation of medicines

- All medicines must be authorized before they can be marketed and made available to patients
- In the EU, there are two main routes for authorizing medicines:
  - Centralized authorization procedure
    - Pharmaceutical companies submit a **single marketing-authorization application** to EMA
  - National authorization procedures
    - Pharmaceutical companies submit a **marketing-authorization application** to specific member country of EU

# MHRA UK

Medicines & Healthcare Regulatory Agency

The MHRA's mission is to enhance and safeguard the health of the public by ensuring that medicines and medical devices work, and are acceptably safe.

# Functions of MHRA

- Regulation of Clinical Trials
- Safety & Efficacy Monitoring
- Information to Public
- Licensing
  - Manufacturer & Dealer Licenses
  - Clinical Trial Licenses
  - Parallel Import Licenses
- Enforcement of Law

# Aims of MHRA

The Agency's aims are:

- Protecting public health through regulation, with acceptable benefit-risk profiles for medicines and devices;
- Promoting public health by helping people who use these products to understand their risks and benefits;
- Improving public health by encouraging and facilitating developments in products that will benefit people.

# Activities of MHRA

Assessing the safety, quality and efficacy of medicines, and authorizing their sale or supply in the UK for human use;

- Overseeing the UK Notified Bodies that audit medical device manufacturers;
- Operating vigilance and other systems for reporting, investigating and monitoring adverse reactions to medicines, medical devices, and blood and blood products, and taking necessary action through safety warnings, removing or restricting the availability of products

# Activities of MHRA

- Operating a quality surveillance system to sample and test medicines, monitoring the safety and quality of imported unlicensed medicines and investigating Internet sales and potential counterfeiting of medicines;
- Regulating clinical trials of medicines and medical devices;
- Monitoring and ensuring compliance with statutory obligations relating to medicines and medical devices through inspection, taking enforcement action where necessary;
- Promoting good practice in the safe use of medicines and medical devices;

# PMDA Japan

PMDA (Pharmaceuticals and Medical Devices Agency) is Japanese regulatory agency, working together with Ministry of Health, Labour and Welfare

PMDA

*stands for*

**Pharmaceuticals and Medical Devices Agency**

The agency established on **April 1, 2004**

# Objectives of PMDA

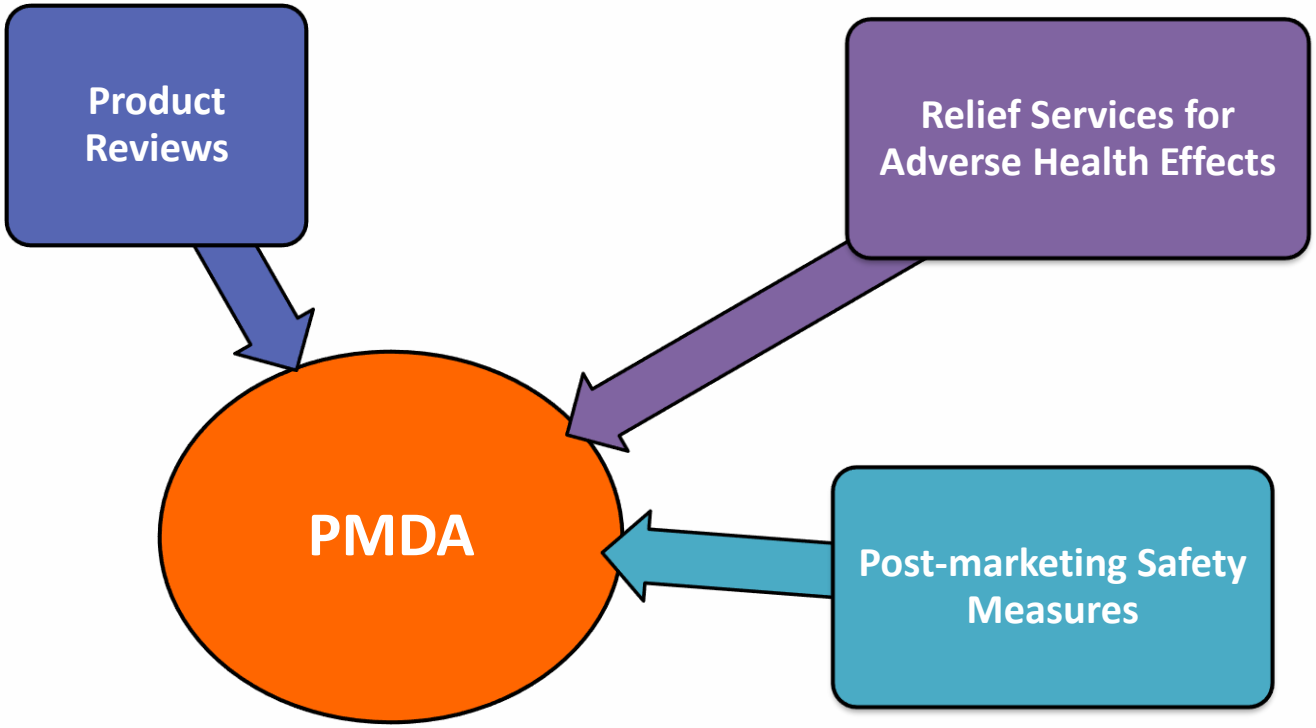
- To pursue the development of medical science while performing duty with greater transparency based on mission to protect public health and the lives of Japanese citizens
- Be the bridge between the patients and their wishes for faster access to safer and more effective drugs and medical devices

# Objectives of PMDA

- Make science-based judgments on quality, safety, and efficacy of medical products by training personnel to have the latest technical knowledge and wisdom in their field of expertise.
- Play an active role within the international community by promoting international harmonization.
- Conduct services in a way that is trusted by the public based on our experiences from the past.

# Services of PMDA

Safety Triangle: Comprehensive Risk Management through the Three Functions



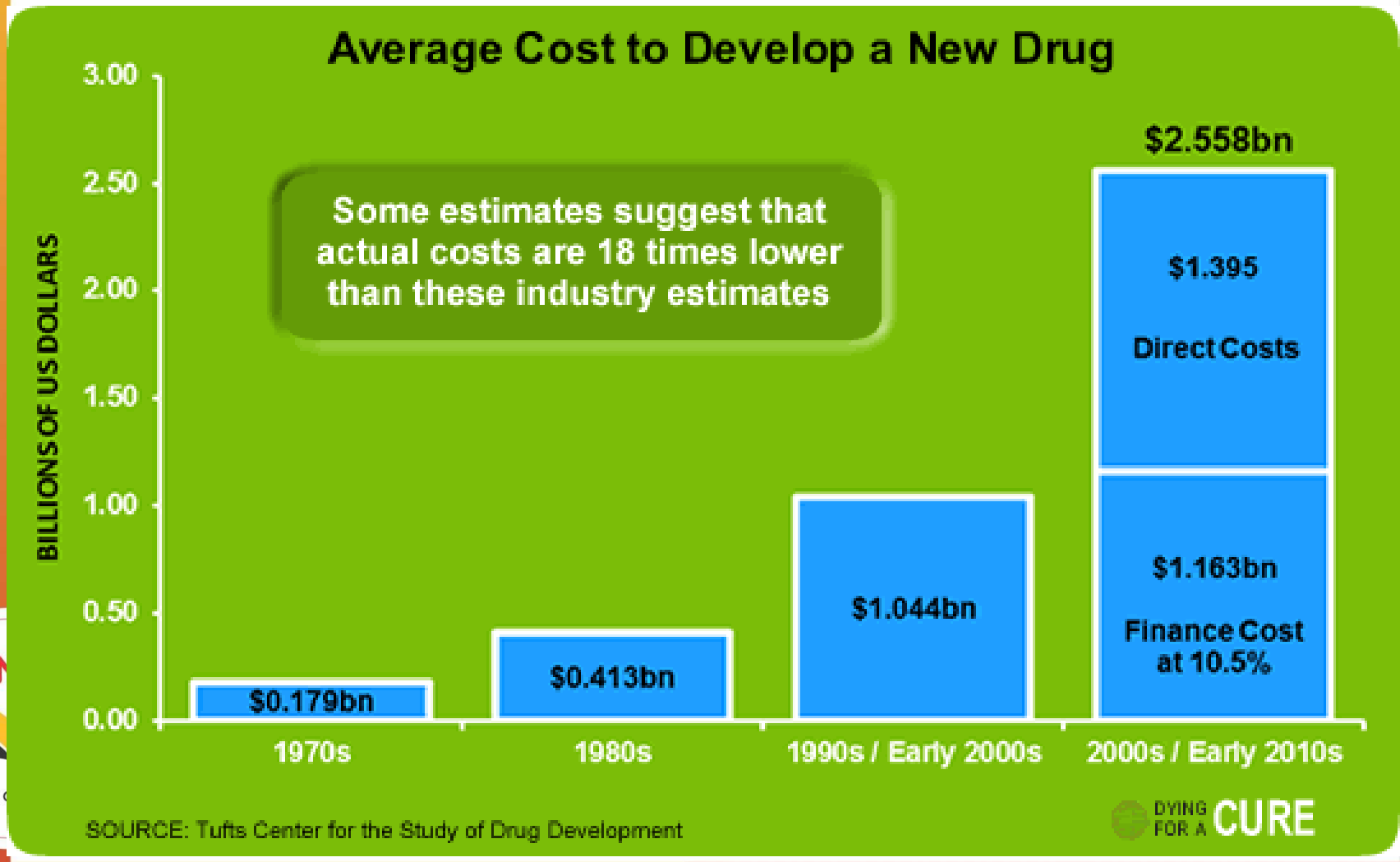
# Confusing Regulations


"I find this new road layout a little confusing."

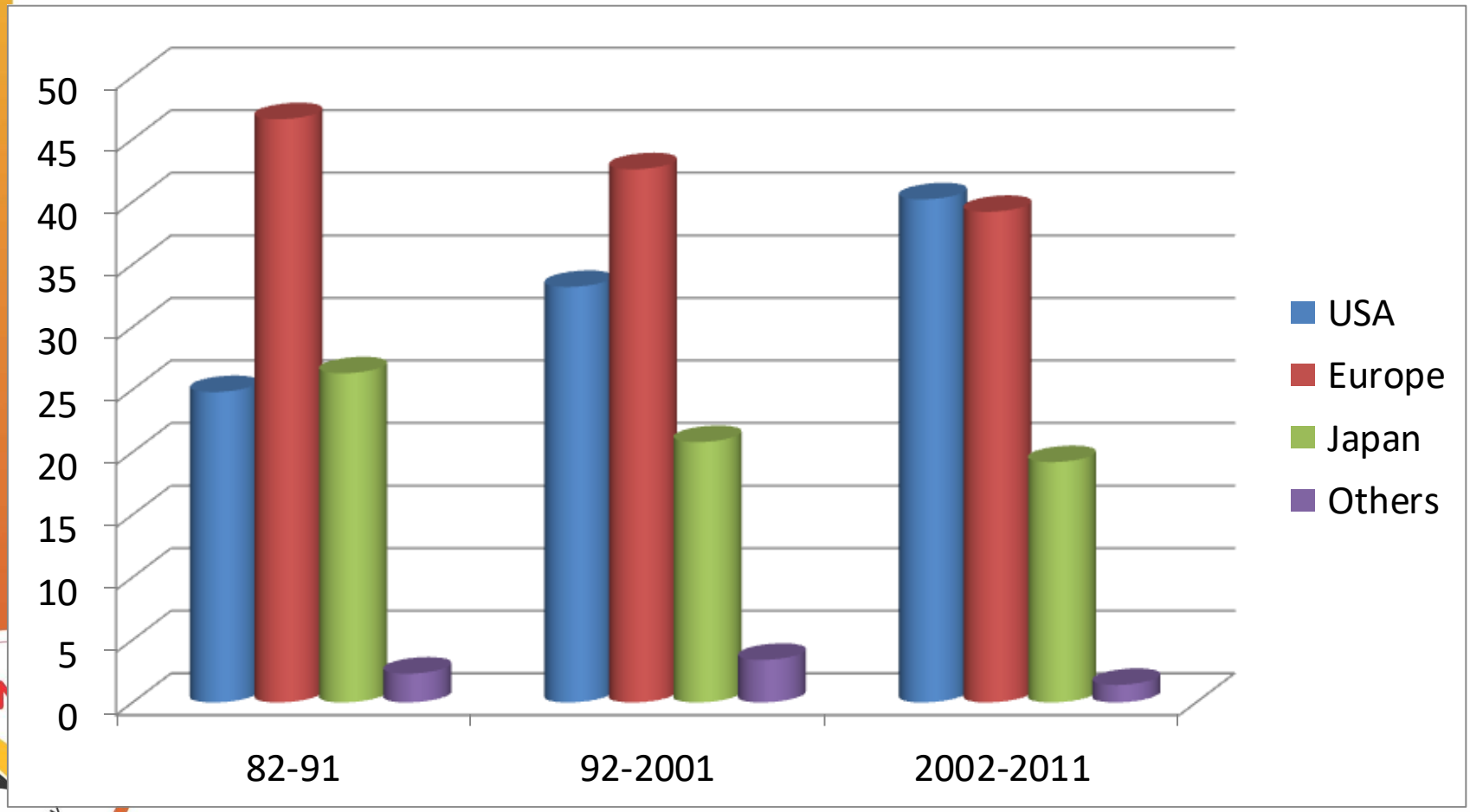
More laws less justice
-Pliny

# Language Barriers

# Drug Development Cost



# Drug Development by Source



# Population & Pharmaceutical Sales

| S.No | Region | Population (Million) | % | Sales ($ b) | % |
|---|---|---|---|---|---|
| 1 | The World | 7410 | 100 | 881 | 100 |
| 2 | N. America | 229 | 3.09 | 349 | 37.3 |
| 3 | Europe | 729 | 9.83 | 221 | 25.1 |
| 4 | Japan | 127 | 1.7 | 112 | 12.7 |
| 5 | 2+3+4 | 1085 | 14.6 | 662 | 75.1 |

ICH

# International Council for Harmonization

*It is a joint initiative involving regulators & industry as equal partners in the scientific & technical discussions of the testing procedures which are required to ensure and assess the safety, quality & efficacy of medicines.*

# Structure

- Three countries, USA, Japan and EU, with their 6 founding member parties (EU, EFPIA, MHLW, JPMA, FDA and PhRMA)
- Observers (WHO, EFTA, Canada) - Non-voting members. India granted observer status in June 2016.
- IFPMA representative

- ICH operates via the ICH Steering Committee, i.e. 6 parties & IFPMA.

# International Council on Harmonization

# ICH Guidelines

Finalized Guidelines:

- Efficacy ($E_1$ to $E_{18}$) GCP=$E_6$ (1996)
- Quality ($Q_1$ to $Q_6$)
- Safety ($S_1$ to $S_7$ & $M_3$)
- Multidisciplinary ($M_1$, $M_2$, $M_4$)

# Efficacy Guidelines

**E1 Clinical Safety for Drugs used in Long-Term Treatment**

**E2A - E2F Pharmacovigilance**

**E3 Clinical Study Reports**

**E4 Dose-Response Studies**

**E5 Ethnic Factors**

**E6 Good Clinical Practice**

**E7 Clinical Trials in Geriatric Population**

**E8 General Considerations for Clinical Trials**

**E9 Statistical Principles for Clinical Trials**

**E10 Choice of Control Group in Clinical Trials**

**E11 Clinical Trials in Pediatric Population**

**E12 Clinical Evaluation by Therapeutic Category**

**E14 Clinical Evaluation of QT**

**E15 Definitions in Pharmacogenetics / Pharmacogenomics**

**E16 Qualification of Genomic Biomarkers**

**E17 Multi-Regional Clinical Trials**

**E18 Genomic Sampling**