Development of GCP

ICH and Indian

Module 1 Topic 4

Multiple Rules

- There was a rapid growth of rules in different countries regarding drug safety and efficacy.
- Drug registration was grossly hampered because of conflicting requirements.
- Repetition of studies using different methods delayed drug developments and increased costs.

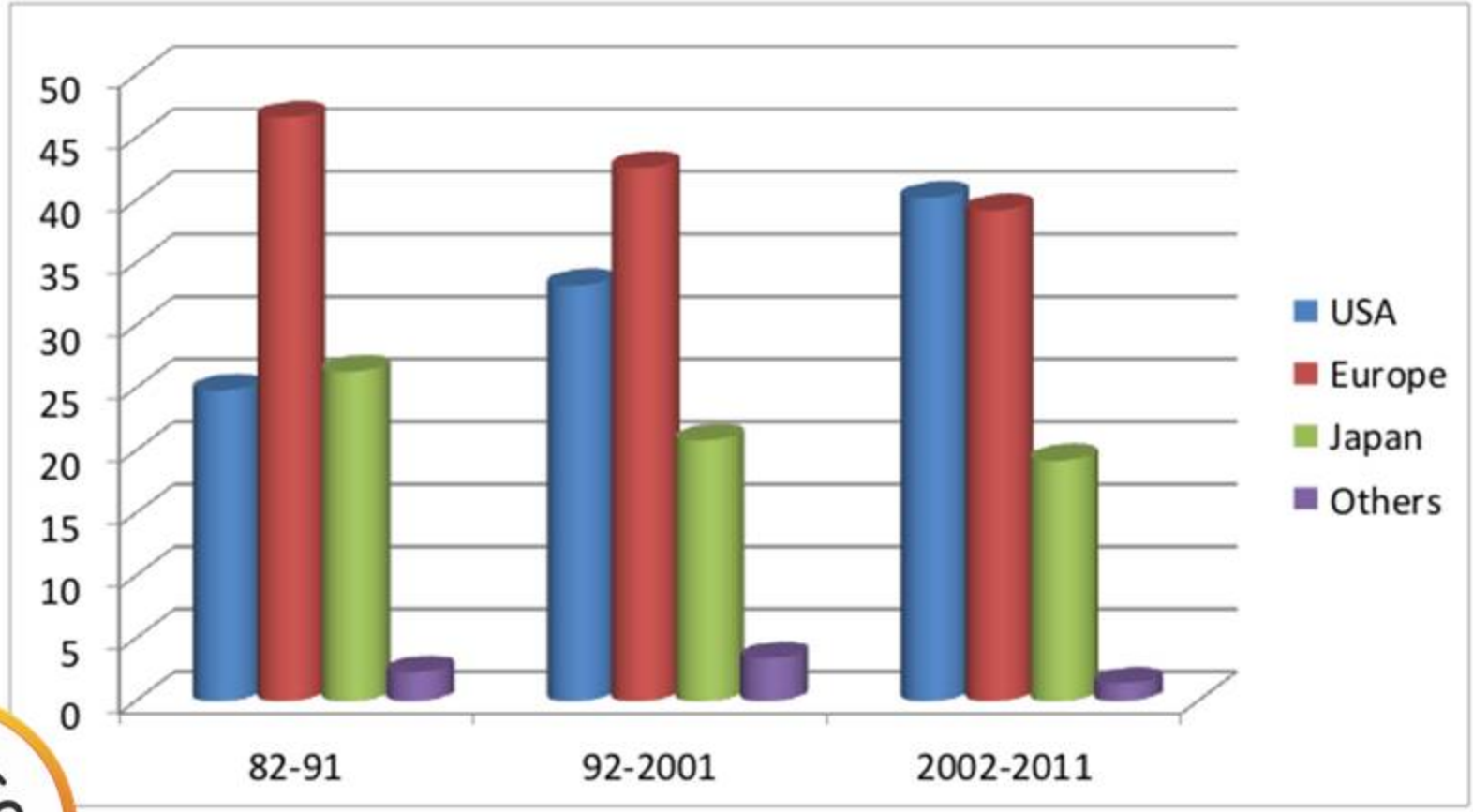
Linguistic chauvinism

- This phenomenon exists in many countries and they want all submissions in their official language.
- Europe has 24 officially recognized languages in addition to English.
- Sponsors were required to translate INDs and NDAs in 10 languages to access European markets.

International Council of Harmonization

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

Drug Development by Source



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

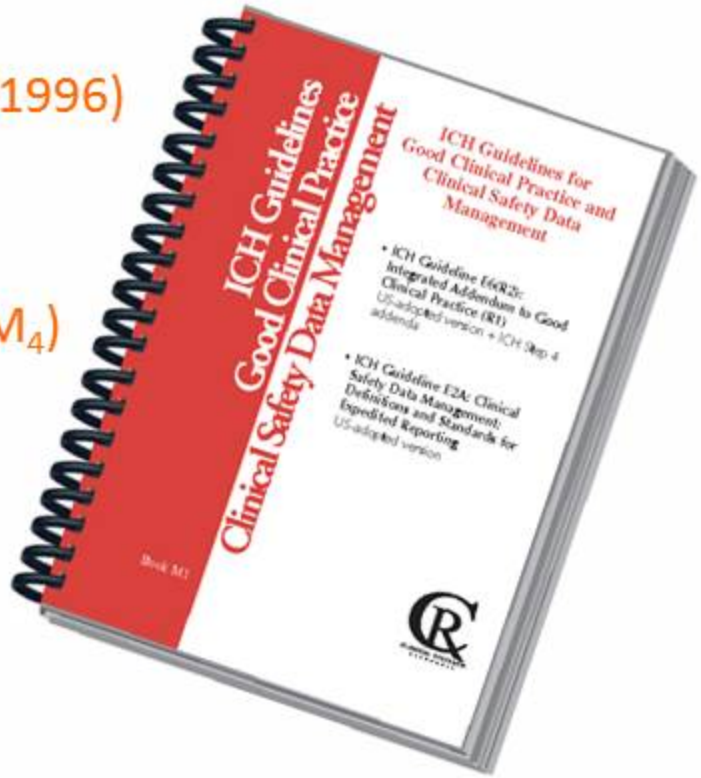
Structure

- Three regions, USA, Japan and EU, with their 6 founding member parties (EU, EFPIA, MHLW, JPMA, FDA and PhRMA)
- Observers (WHO, IFPMA, Canada) - Non-voting members. India granted observer status in June 2016.
- ICH operates via the ICH Steering Committee, i.e. 6 parties & IFPMA.

International Council on Harmonization

ICH

- Finalized Guidelines:
  - Efficacy (E_1 to E_{12}) 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

Efficacy Guidelines

- 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

E 6 GCP History

- **(R1)** Adopted by CPMP, July 1996
- Revision Draft **(R2)** released in June 2015
- Currently Step 4
- Changes in Chapters:
    1. Introduction,
    2. Glossary
    4. Investigator
    5. Sponsor
    8. Essential Documents

Good Clinical Practice (GCP)

- An international ethical and scientific quality standard for designing, conducting and reporting clinical trials that involve the participation of human subjects.

- Provides public assurance that rights, safety & well-being of trial subjects are protected, consistent with Declaration of Helsinki and that the **clinical** data are credible.

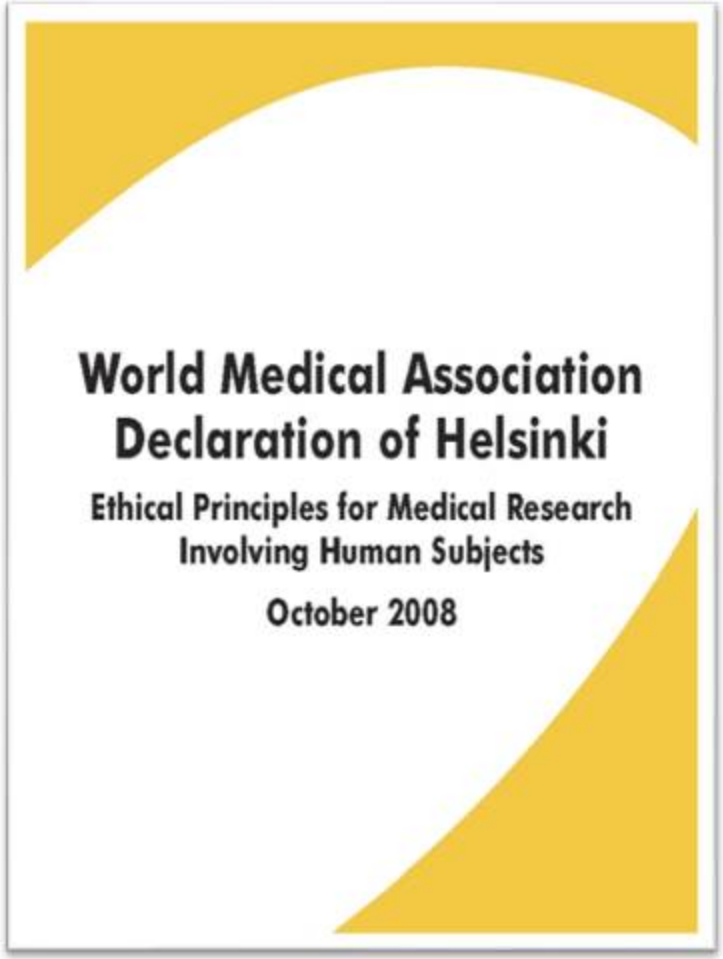
ICH-GCP

Table of Contents - 8 sections

1. Glossary
2. The Principles of ICH-GCP
3. Institutional Review Board/Independent Ethics Committee (IRB/IEC)
4. Investigator
5. Sponsor
6. Clinical Trial Protocol & Protocol Amendment(s)
7. Investigator's Brochure
8. Essential Documents for Conduct of a Clinical Trial

Principles of ICH GCP

2.1 Clinical trials to be conducted in accordance with ethical principles that have their origin in the DoH & consistent with GCP & regulatory requirement(s).



Principles of ICH GCP

2.2 Foreseeable risks & inconveniences to be weighed against the anticipated benefit for the individual trial subject & society.

Principles of ICH GCP

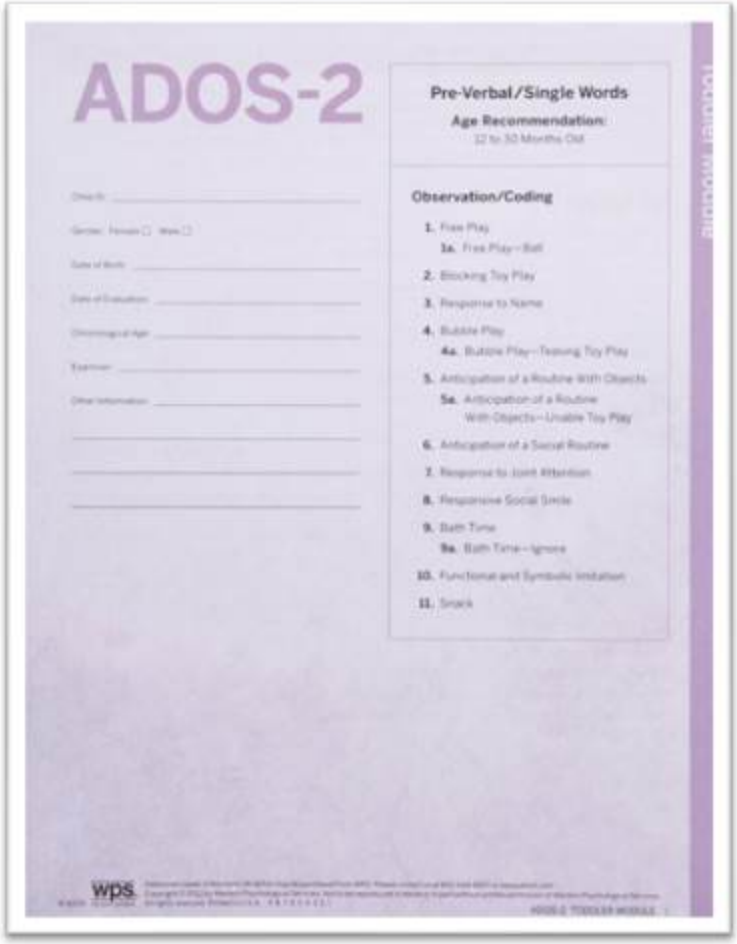
2.3 The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.

Principles of ICH GCP

2.4 The available non-clinical and clinical information on an investigational product should be adequate to support the proposed trial.

Principles of ICH GCP

2.5 Clinical trials should be scientifically sound, and described in a clear, detailed protocol.



Principles of ICH GCP

2.6 A trial should be conducted in compliance with the protocol that has received prior IRB/IEC approval/favourable opinion.

Principles of ICH GCP

2.7 The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician.

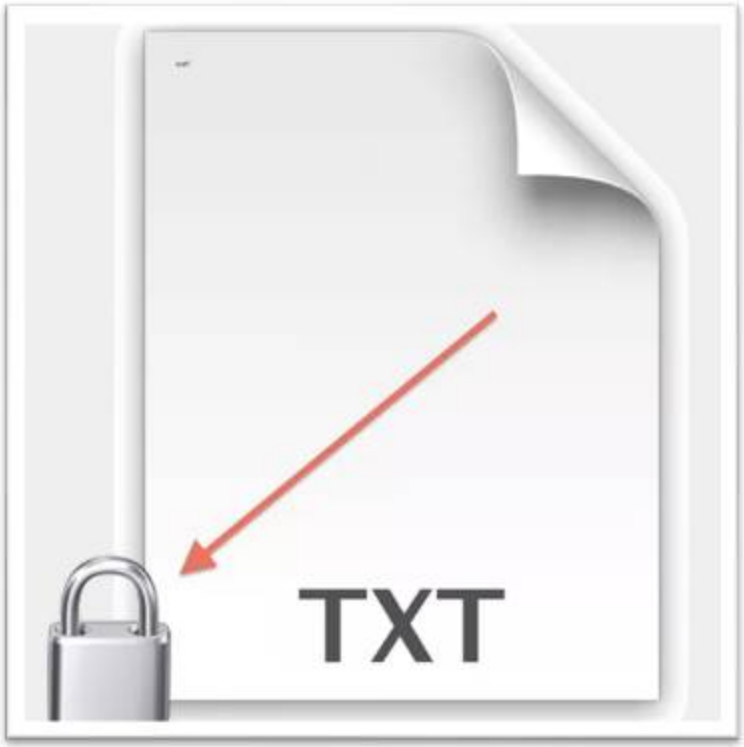
Principles of ICH GCP

2.8 Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his/her respective task(s).

2.9 Freely given informed consent should be obtained from every subject prior to clinical trial participation.

Principles of ICH GCP

2.10 All trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.



Principles of ICH GCP

2.11 Confidentiality of records that could identify subjects should be protected.

Principles of ICH GCP

2.12 Investigational products should be manufactured, handled, and stored in accordance with Good Manufacturing Practice (GMP).

Principles of ICH GCP

2.13 Systems with procedures that assure quality of every aspect of trial should be implemented.

Federal Structure

Central Government	Concurrent List	State Government
97 items	52 items	61 items

Federal Structure – applicable to Pharmaceuticals

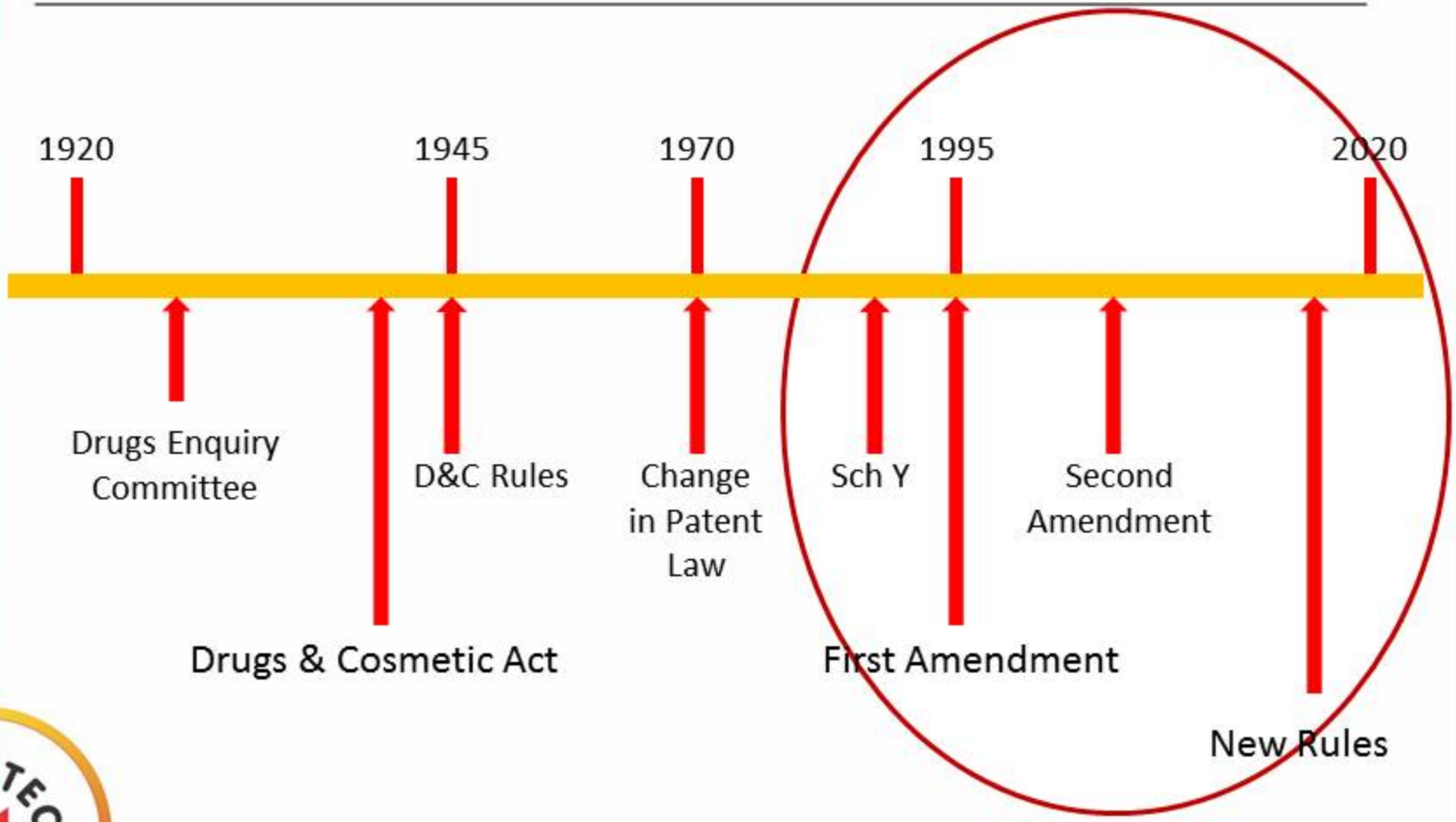
Central Government

- Import
- Export
- New Drugs

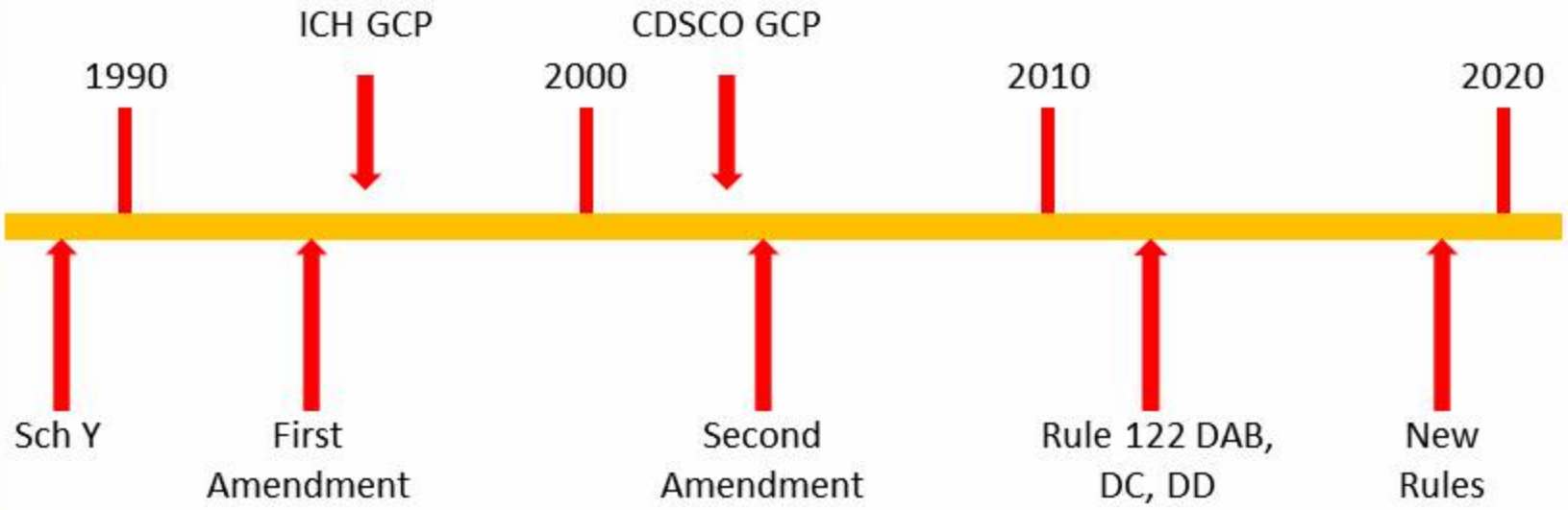
State Government

- Manufacture
- Distribution
- Sale

Time Lines


1920
1945
1970
1995
2020
Drugs Enquiry Committee
Drugs & Cosmetic Act
D&C Rules
Change in Patent Law
Sch Y
First Amendment
Second Amendment
New Rules

The Regulation Timeline



CDSCO GCP Contents

1. Definitions
2. Pre Study Requisites
   - 2.1 Investigational Pharmaceutical Product
   - 2.2 Pre clinical supporting data
   - 2.3 Protocol
   - 2.4 Ethical and safety considerations
3. Responsibilities
   - 3.1 Sponsor
   - 3.2 The Monitor
   - 3.3 Investigator

CDSCO GCP Contents

4. Record keeping and data handling
5. Quality assurance
6. Statistics
7. Special concerns

Appendices

I. Declaration of Helsinki
II. Schedule Y
III. Format for submission of pre clinical and clinical data on rDNA based vaccines, diagnostics & biologicals
IV. Investigator's Brochure
V. Essential documents

CDSCO GCP

- Main differences from ICH GCP
  - Glossary of terms given as definition of terms
  - Differences in EC constitution and responsibilities
  - Compensation requirements well defined
  - Guidance on documents required for application for initiation of clinical trials or for permission for marketing included.
  - Animal study requirements included
  - Details of clinical trial phases included
  - Sections on trials of contraceptives, vaccines, herbal drugs, surgical procedures, devices, radioactive materials and X rays.

Multiplicity of Rules

- CDSCO GCP Guidelines
- Schedule Y
- ICMR Ethics Guidelines
- Draft of New Drugs and Clinical Trial Rules 2018 published in Feb 2018, they will replace Part XA and Schedule Y of the Drug and Cosmetics Rules 1945