

# Good Clinical Practice GCP

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## Good Clinical Practice (GCP)

“A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.”

# History



# GCP History

## 1938 US Food Drug and Cosmetic Act

- Sulfanilamide
- Anti-streptococcal agent
- Paediatric syrup
  - Dissolved in ethylene glycol
- > 100 people died
- Act required animal safety testing and submission of data to FDA





## GCP History

### 1947 Nuremberg - The Doctors Trial

- Performing medical experiments, without the subjects' consent
- Experiments
  - Freezing – hypothermia
  - Malaria – treatment
  - Sea water – desalination techniques
  - Sterilisation – effective techniques



# GCP History

## 1947 Nuremberg code – 10 key points

- Voluntary consent is essential
- Unnecessary suffering should be avoided
- The experiment should be conducted only by scientifically qualified persons
- Subject has the liberty to stop the experiment



# GCP History

## 1961 Thalidomide

- Marketed as a sedative with remarkably few side effects
- Prescribed to pregnant women to help combat morning sickness
- >10,000 children were born with severe malformations



# GCP History

## 1962 Kefauver Harris Amendments

- Inadequate safety data, both pre-clinical and clinical – Frances Kelsey
- Proof of safety and efficacy





## GCP History

- 1964 Declaration of Helsinki
- 1977 FDA implements GCP
- 1986 UK implements GCP
- 1989 Nordic countries implement GCP
- 1990 EU implements GCP
- 1996 ICH Guidelines for Good Clinical Practice - GCP



## GCP History

- 2001 EU Directive 2001/20/EC “Clinical Trials Directive”
- 2004 EU Directive implemented in national legislation
- 2005 Directive 2005/28/EC “GCP Directive”



## GCP History

- 2006 TeGenero/TGN1412
- 2007 New EU guidance:  
“Guideline on strategies to identify and minimise risks for first-in-human clinical trials with investigational medicinal products”

# Declaration of Helsinki 1964



## **WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI Ethical Principles for Medical Research Involving Human Subjects**

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the:  
29th WMA General Assembly, Tokyo, Japan, October 1975  
35th WMA General Assembly, Venice, Italy, October 1983  
41st WMA General Assembly, Hong Kong, September 1989  
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996  
52nd WMA General Assembly, Edinburgh, Scotland, October 2000  
53rd WMA General Assembly, Washington 2002 (Note of Clarification on paragraph 29 added)  
55th WMA General Assembly, Tokyo 2004 (Note of Clarification on Paragraph 30 added)  
59th WMA General Assembly, Seoul, October 2008





## Declaration of Helsinki

- Statement of ethical principles
- Not legally binding
- Duty of the physician to safeguard the health of his patient





## Declaration of Helsinki

“It is the duty of physicians who participate in medical research to protect the

- Life
- Health
- Dignity
- Integrity
- Right to self-determination
- Privacy, and
- Confidentiality of personal information of research subjects”





## Declaration of Helsinki

- Participation by competent individuals as subjects in medical research must be voluntary
- In medical research involving competent human subjects, each potential subject must be adequately informed
- The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal

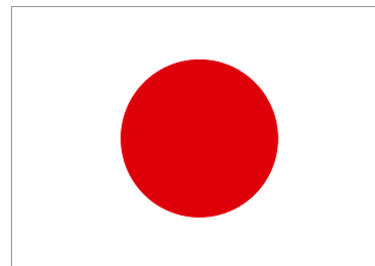


# ICH Guideline E6, GCP



# ICH – The International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use

Unified standard for the EU, Japan and the USA to  
facilitate the mutual acceptance of clinical data





# ICH

## Regulators

- EU European Commission (EC)
- Japan Ministry of Health, Labour & Welfare (MHLW)
- USA Food & Drug Administration (FDA)

## Pharma

- EFPIA  
European Federation of Pharmaceutical Industries' Associations
- JPMA  
Japan Pharmaceutical Manufacturers Association
- PhRMA  
Pharmaceutical Research & Manufacturers of America





## ICH Guidelines

- Q - Quality
- E - Efficacy
- S – Safety
- M - Multidisciplinary





## ICH E Guidelines

- E1: Extent of population exposure to assess safety
- E2: Safety reporting (E2A, B, C, D, E and F)
- E3: Clinical study reports
- E4: Dose response information
- E5: Ethnic considerations in the acceptability of foreign data
- **E6: GCP guidelines**
- E7: Clinical Trials in Special Populations - Geriatrics





# ICH E Guidelines

- E8: General Considerations
- E9: Statistical Principles
- E10: Choice of Control Group
- E11: Studies in children
- E12: Therapeutic area guidelines
- E14: Clinical Evaluation for Anti-Arrhythmic Drugs
- E15: Definitions for Genomic Biomarkers
- E16: Genomic Biomarkers Related to Drug Response





INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL  
REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN  
USE

**ICH HARMONISED TRIPARTITE GUIDELINE**

**GUIDELINE FOR GOOD CLINICAL PRACTICE  
E6(R1)**

Current *Step 4* version  
dated 10 June 1996





## Why GCP?

- Provides a unified standard to facilitate the mutual acceptance of clinical data by the regulatory authorities
- Protects the rights, safety and integrity of the study subjects
- Assurance of credible and accurate data





## ICH E6 GCP - contents

1. Glossary
2. Principles of GCP
3. Independent Ethics Committee
4. Investigator
5. Sponsor
6. Clinical Trial Protocol and Amendments
7. Investigator's brochure
8. Essential documents





## Principles of ICH GCP

1. Clinical trials should be conducted in accordance with the ethical principles in the Declaration of Helsinki and that are consistent with GCP and applicable regulatory requirement(s)
2. Anticipated benefits justify the risks
3. The rights, safety, and well-being of the trial subjects are the most important considerations and prevail over the interests of science and society



## Principles of ICH GCP

4. Adequate non-clinical and clinical information
5. Scientifically sound, and described in a clear, detailed protocol
6. Compliance with the protocol, as approved by IEC
7. Medical care/decisions – responsibility of qualified physician



## Principles of ICH GCP

8. Each individual should be qualified by training and experience
9. Freely given informed consent, from every subject prior to trial participation
10. Data handling to allow accurate reporting



## Principles of ICH GCP

11. Respect of privacy and confidentiality
12. IPs - in accordance with GMP
13. Procedures that assure quality should be implemented



*Guideline for Good Clinical Practice*

**8.2 Before the Clinical Phase of the Trial Commences**

During this planning stage the following documents should be generated and should be on file before the trial formally starts

	<b>Title of Document</b>	<b>Purpose</b>	<b>Located in Files of</b>	
			<b>Investigator/ Institution</b>	<b>Sponsor</b>
8.2.1	<b>INVESTIGATOR'S BROCHURE</b>	To document that relevant and current scientific information about the investigational product has been provided to the investigator	X	X
8.2.2	<b>SIGNED PROTOCOL AND AMENDMENTS, IF ANY, AND SAMPLE CASE REPORT FORM (CRF)</b>	To document investigator and sponsor agreement to the protocol/amendment(s) and CRF	X	X
8.2.3	<b>INFORMATION GIVEN TO TRIAL SUBJECT</b>		X	X
	- <b>INFORMED CONSENT FORM</b> (including all applicable translations)	To document the informed consent		
	- <b>ANY OTHER WRITTEN INFORMATION</b>	To document that subjects will be given appropriate written information (content and wording) to support their ability to give fully informed consent	X	X
	- <b>ADVERTISEMENT FOR SUBJECT RECRUITMENT</b> (if used)	To document that recruitment measures are appropriate and not coercive	X	
8.2.4	<b>FINANCIAL ASPECTS OF THE TRIAL</b>	To document the financial agreement between the investigator/institution and the sponsor for the trial	X	X

# EU Directives



## Key EU Directives

- 2001/20/EC "Clinical Trials Directive"
- 2005/28/EC "GCP Directive"
- 2003/94/EC "GMP Directive"

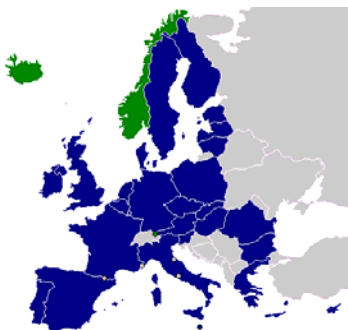




## 2001/20/EC



- All trials to be performed to detailed GCP guidelines that are internationally recognised and laid down by the Commission – implies ICH GCP
- Mandatory inspections to check GCP and GMP compliance
  - (since 01.05.04 = 1552 01.01.10)





## Directive 2001/20/EC

- Authorisation from CAs
- EudraCT database
- Ethics committee approval
- Consent
- Safety reporting
- IPs
- Inspections



## Directive 2005/28/EC

- GCP Principles
- TMF and archiving
- Qualifications of Inspectors
- Inspection procedures
- Manufacturing/Import Authorisation for IPs



# Factors Affecting Trials

National  
Laws

Voluntary  
Codes

Declaration  
of Helsinki

ICH  
Guidelines

Clinical  
Trial

Data  
Protection

CTs /GCP  
Directives

Inspections

FDA  
Regulations



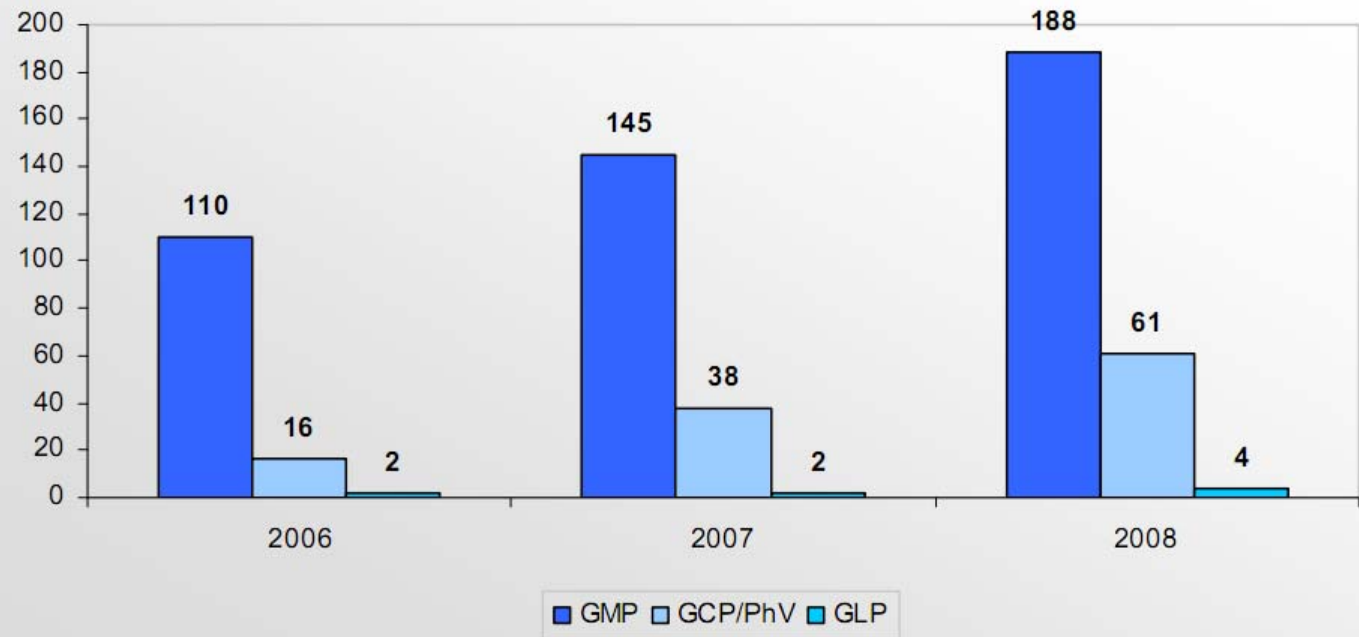
## Inspections

- National CAs
- EMA
- FDA
- Japanese inspectors
- GCP
- GLP
- GMP
- PhV



# EMA Inspections

Number of inspections (2006-2008)





## Useful websites

- [http://ec.europa.eu/enterprise/sectors/pharmaceuticals/documents/eudralex/vol-10/index\\_en.htm](http://ec.europa.eu/enterprise/sectors/pharmaceuticals/documents/eudralex/vol-10/index_en.htm)
- <https://eudract.emea.europa.eu/>
- <http://www.legemiddelverket.no/>




Om Legemiddelverket | Kontakt | Nettkart | Presse | Abonnement | English | Jobb i Legemiddelverket

**Statens legemiddelverk**  
Norwegian Medicines Agency


Forside
Forbruker
Helsepersonell
Apotek og grossist
Industri

**▶ Forbruker**  
Aktuelle hurtigvalg:


- [Følg oss i sosiale medier:](#)




- [Byttbare legemidler](#)
- [Medisiner på utenlandsreise](#)
- [Naturlegemidler](#)
- [Sant og usant om legemidler og naturmidler](#)
- [Netthandel](#)
- [P-piller](#)
- [Melanotan](#)
- [Vaksine mot livmorhalskreft](#)

**Aktuelt**

[Legemiddelverket presiserer: \(25.02.2010\)](#)




Det er ingen endringer i loverket for innførsel av legemidler til personlig bruk fra utlandet. Det nye er at endringer i apotekloven har åpnet for at apotekene kan drive nettapotek i Norge og forsende reseptfrie legemidler uten geografiske begrensninger.

[Mangel på Phenamin mikstur \(24.02.2010\)](#)



Grunnet leveringsproblemer for Phenamin mikstur "Nycomed" har Statens legemiddelverk bestemt at apotekene inntil videre kan levere ut deksklorfeniramin mikstur i utenlandske pakninger. Det er ikke nødvendig å søke om spesielt godkjenningfritak.


[Rådsavgjørelse 08.02.2010: Bayer får gebyr for Qlaira-reklame \(24.02.2010\)](#)




Legemiddelverket mente at markedsføringsmaterieell for p-pillen Qlaira ikke var balansert og klaget til Rådet for legemiddelinformasjon. Legemiddelfirmaet Bayer fikk et gebyr på 60 000 kroner. – Vi er glade for at Rådet støtter vårt syn i denne saken, sier seniorrådgiver Bente Jerkø.

- [Bivirkningsrapporter registrert ved Pandemrix – uke 7 \(19.02.2010\)](#)
- [Urtebasert kosttilskudd – vær kritisk! \(17.02.2010\)](#)
- [FEST version 1 erstattes av version 2 \(16.02.2010\)](#)

Informasjon i forbindelse med ny influensa H1N1

**Legemiddelsøk**


**Meld bivirkninger**


**Nytt om legemidler**


**Legemiddelanmeldelser**

Likeverdige medisiner – trygt medisinbytte i apotek



Thank You