EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Clinical Trials for Medicines and Ethics: the European Union Regulations

Isabel de la Mata
Principal Advisor for Public Health
European Commission

EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Clinical Trials Directive

- Directive 2001/20/EC on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use
- Entered into force 1 May 2004
- Commission Directive 2005/28/EC laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products

Directorate-General for Health & Consumers

Clinical trials regulation
How? vs. What?

How is clinical research with pharmaceuticals conducted in order to ensure

- Patient rights
- Patient safety
- Data reliability

➔ ***CLINICAL TRIALS DIRECTIVE***

What clinical research has to be conducted to obtain a marketing authorisation or to have rewards?

➔ ***Requirements for application for marketing authorisation (Directive on medicinal products)***

Key issues:

Safety of participants
Rights of participants
Reliability and robustness of data

These aims are valid independently of the qualification of the sponsor as “commercial”/”non-commercial”!

EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Protection of participants

- Protection of human rights and dignity of the human being with regard to the application of biology and medicine
- Rights of the subject to physical and mental integrity
- Risk assessment (prior toxicological experiments)
- Screening (ethics committees and authorities)
- Right to privacy and to protection of personal data
- Withdraw
- Insurance/indemnity

Main concepts:

- ‘Authorisation’ by national competent authority and Ethics Committee in every Member State concerned
- Rules on
  - Responsibilities of sponsor and investigator
  - Authorisation procedure
  - Informed consent
  - Adverse events/reactions reporting
  - Inspections
  - Manufacturing and importation of IMP
  - EudraCT - database

EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Clinical trial definition

- Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product (s), and/or identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy

EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Scope

- Medicinal products
- Commercial and non-commercial
- Includes multicentre trials
- Not apply to non-interventional trials
- Good clinical practice (designing, conducting, recording, transmitting)

EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Informed consent

- Written
- Dated
- Signed
- Free
- Informed

- Persons incapable of giving legal consent: only if direct benefit
- Children
- Legal representatives: national law
- The interests of the patient always prevail over those of science and society

Ethics Committee

- Member State
- Opinion before commencement of the clinical trials
- Time for opinion
- Single opinion for 1 MS
- If multicountry, 1 opinion for MS
- Always informed if trial suspended or suspected serious unexpected adverse reactions

EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Commission Directive 2005/28/EC

- Detailed guidelines of good clinical practice to protect trial subjets and ensure no unnecessary clinical trials conducted
- Functioning of the Ethics Committees

EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Good clinical practice

- The rights, safety and well being of the trial subjects shall prevail over the interests of science and society
- Clinical trials shall be scientifically sound and guided by ethical principles in all ther aspects
- The necessary procedures to secure the quality of every aspects of the trials shall be complied with
- Accordance with the Declaration of Helsinki on Ethical Principles for Medical Reseach Involving Human Subjects (1996).

EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Ethics Committees

- MS
- Keep documentation
- Communication with competent authorities of MS

Other Guidelines

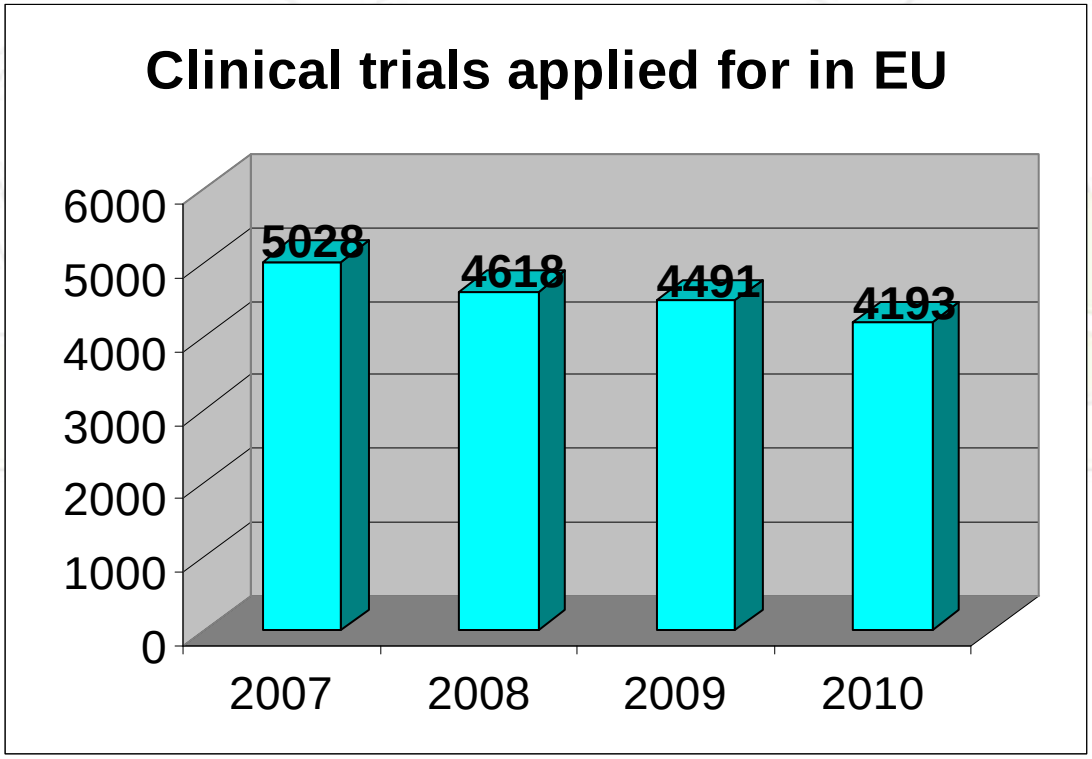
- European Commission: Vol 10 EudraLex: the rules governing medicinal products in the EU
- EMA
- Heads of Medicines Agencies: Clinical Trials Facilitation group

EudraLex

- Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial (March 2010)
- Detailed guidance on the application format and coumentation to be submitted in an application for an Ethics Committee opinion on the clinical trial on medicinal products for human use (February 2008)
- Other on Monitoring and Pharmacovigilance, Quality of the Investigational Medicinal product and Inspections

Some figures

- Approx. 4.200 clinical trials per year in EU applied for
- 8.000 clinical trial *applications* per year
- 400.000 EU-participants planned for enrolment


Clinical trials applied for in EU
6000
5000
4000
3000
2000
1000
0
5028
4618
4491
4193
2007
2008
2009
2010

EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Transparency of Clinical Trials

https://www.clinicaltrialsregister.eu

Since March 2011: Public official Clinical Trials Register

Contains all authorised clinical trials (except certain phase-1 trials)

EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Revision of Directive - State of play

- Communication 10 Dec 2008 on "Safe, Innovative and Accessible Medicines; a renewed Vision for the Pharmaceutical Sector": assessment of the 2001Directive
- Public consultation until January 2010. Published
- Roadmap of the Commision impact assessment, setting out the main structure and the next steps
- Public consultation on a concept paper on the revision of the Clinical Trials Directive, launched on February 20112 public consultations. Responses published
- Legislative proposal by COM in 2012
- Submission to co-legislators who may accept, amend, or reject the proposal

EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Scope

- No change of scope
- No exclusion of low risk trials
- No exclusion of "academic/non commercial sponsors"

EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Practical requirements

- More detailed risk-adapted provisions on content of the application, dossier and safetyy reporting
- System of indemnisation
- "Emergency clinical trials"

EUROPEAN COMMISSION

Directorate-General for Health & Consumers

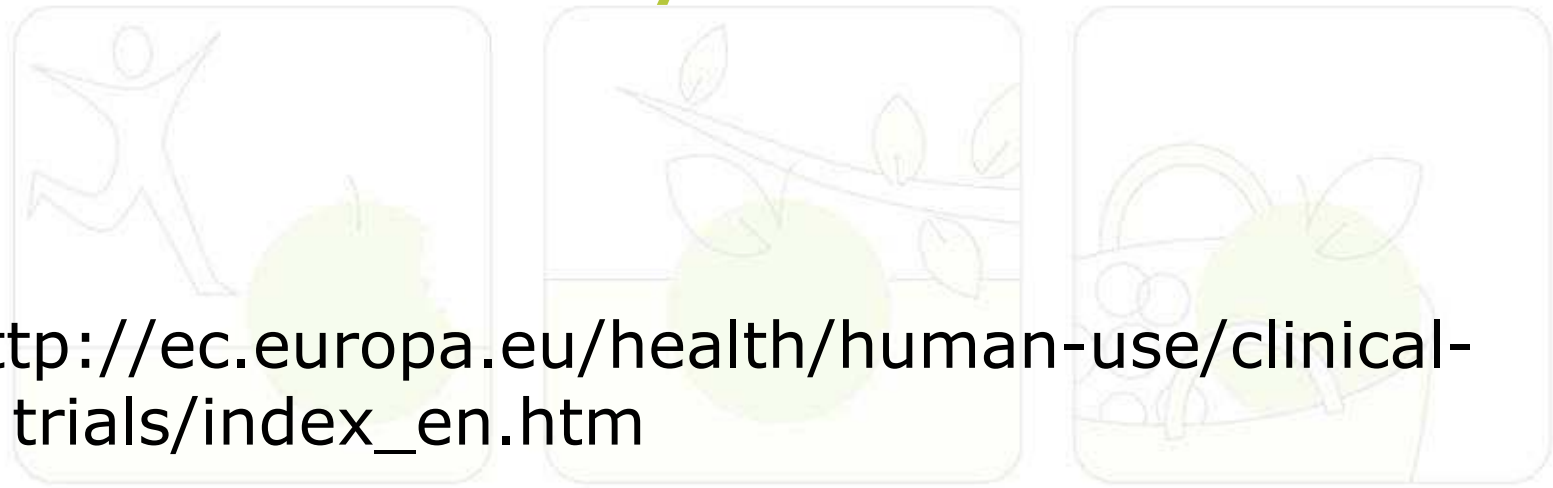
Third countries

- Ensure compliance with Good Clinical Practices in clinical trials performed in third countries
- Increase transparency

EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Many thanks!



http://ec.europa.eu/health/human-use/clinical-trials/index_en.htm