New Clinical Trial Regulation and clinical research in Academia

Elke Stahl
CoChair CTFG

Bundesinstitut
für Arzneimittel
und Medizinprodukte

Clinical Trial Facilitation Group
CTFG

Why need to regulate Clinical Trials?

- A Clinical Trial (CT) can be conducted, if
  - The **rights, safety, dignity, and well-being** of **SUBJECTS are protected** and prevail over all other interests
  - It is designed to **generate reliable and robust DATA**

(Art 3, EU Clinical Trial Regulation 536/2014, (CTR))

➢ **Positive benefit risk balance**

What's needed to start a Clinical Trial?

Pre-requisite to conduct a Clinical Trial is

- **Approval** by National Competent Authority NCA) &
- **Positive Opinion** by Ethics Committee

E.g.

- Benefit - Risk : Effect/efficacy (pharmacology)
  versus Safety/tolerability
  dependening on development status
- Suitability : Clinical trial site and investigator
- Recruitment, information of participants, consent, insurance cover
- …… (for details see → Directive/Regulation)

CTFG

What is responsibilities of regulatory bodies?

- Assess and approve **initial CT** application
- Throughout the whole ***life cycle of a CT***
  - **Substantial amendments** – assess and approve
  - **Safety reporting** – follow/assess
    - SUSAR reporting
    - Annual Safety Report (DSUR format)
    - Reference Safety Information (part of IB or SmPC)
  - **Notifications** with potential impact on benefit risk – assess, e.g. new relevant information, class effects, urgent safety measure, serious breaches…

CTFG

Regulatory body : Responsibilities II

- While supervision may ask for ***Corrrective Measure***:
  - Any modification
  - Halt (suspend authorization) or
  - Stop (revoke authorization) of a clinical trial, if the positive benefit risk no longer given
- Initiate and perform **inspection** of a clinical trial (e.g. GCP, pharmacovigilance)
- Status of a CT and final results of a clinical trial uploaded in EU/global **database/register** for transparency to general public

CTFG

Why Clinical Trial Regulation EU 536/2014 (CTR)?

- Europe EU/EEA 30 Member States
  - Directive 2001/20/EC *transferred* into 30 (different) national laws

- Harmonisation in EU/EEA
- Regulation (= replacing national laws for competent authorities and ethic committees in Member States)
- No national interpretations or additions possible
- Control by European Commission
- Simplification for sponsor (not Member States)

CTFG

What is CTR 536/2014 about?

- **Matter of ONE**
  - 1 Single application procedure for mono- and multinational CTs, including substantial modifications
  - 1 Communication hub : ‚EU Portal and database‘
  - 1 Lead MS in part I: Reporting Member State (RMS)
  - 1 Set of documents
  - 1 Joint assessment (part I) of all concerned MS (MSCs)
  - 1 Decision per application per MS
  - 1 Fee per MS

  - Add more MSC after first authorization

CTFG

CTR EU 536/2014 – Other Changes?

- Fixed maximum tight **timelines** in EU
- **New concept of Clinical Study** :
  any investigation in relation to humans intend to indentify:
  a) Pharmacological or pharmacodynamic effects of medical product/s
  b) Adverse reaction to medical product/s
  c) ADME of medical product/s
  - **Clinical Trial**
    a) Asign to therapeutic strategy in advance… not within normal clinical practice of the MSC
    b) Decision to prescripe the IMPs together with decision to include in CT
    c) Diagnostic or monitoring procedure in addition to normal clinical practice
  - **Non interventional clinical trial** is a clinical study but other than clinical trial

CTFG

CTR EU 536/2014 – Other Changes II

- **Low interventional trial**, if
  - IMP is authorized, except placebo
  - IMP used within terms of marketing authorization, or
    - Off-label use is evidence based and supported by published scientifc evidence on safety and efficacy in any MSC
  - Additional diagnostic or monitoring procdures no more than minimal additional risk or burden to the saftey of participants compared to normal clinical practice in any MSC
  - ➢ … Insurance
- **Emergency situations** without prior informed consent
- **Cluster trials**
- **Informed consent** : subjects without decision-making capacity

CTFG

CTR EU 536/2014 – Other Changes III

- **Transparency**: Protocols, results, assessment
  - ➢ Improve Research
- IT system prerequisite to get CTR applicable
  EU Portal and Database (EUPD) training by EMA
- Commission collects survey
  on national support for academic researchers
- MS:
  - ➢ **No change in content of assessment** (jointly)
  - ➢ Change in timelines for all stakeholders
  - ➢ Only one application per CT – One decision per MS

CTFG

Clinical Trial Facilitation Group - CTFG

- Working group of Head of Medicines Agency (HMA)
- Network of NCA's initiated with Directive 2001/20 on CTs in 2004

- Tasks/Actions: The ‚body' for CTs in EU/EEA
  - Support, **harmonize and facilitate CTs in EU/EEA**
    - Develop harmonized **procedures**
    - **Common positions** on regulatory or scientific issues
  - Support development of **guidances**
  - Support **implementation** *of EU CTR 536/2014*
    - *Readiness* of NCAs/MSs for CTR
    - Development of EUPD/CTIS

CTFG

Clinical Trial Facilitation Group - CTFG

- Develop **harmonized (coodinated) procedures**
  - Voluntary harmonisation procedure (VHP)
  - VHPplus (plus Ethics)
  - Annual safety report work sharing
  - Safety relevant issue

- **Common positions on regulatory or scientific issues**, e.g.
  - Contraception in CTs
  - Reference safety information, annual safety report (DSUR)
  - In work - Complex CT design
  - ….

http://www.hma.eu/ctfg.html

CTFG

Clinical Trial Facilitation Group - CTFG

- Support implementation of CTR
  - **Tracking** readiness of NCAs/MSs with ‚traffic lights'
  - **Best Practice** of MSs on procedures, definitions
  - Assessment Report **Templates**
    - Initial draft assessment report (AR) and final AR
    - Annual Safety Report AR
  - **Guidance** support, e.g.
    - COM's risk based approach
    - AxMP (former NIMPs)
    - QnA safety

CTFG

Clinical Trial Facilitation Group - CTFG

…Support implementation of CTR
- Development EU portal and database

- In future, further facilitates CTs in EU/EEA
  - Coordinated harmonisation and opinions
  - Regular exchange with **ALL** stakeholders
    - Burning issues and horizon scan
  - Scientific and regulatory opinions of aspects in CTs of general interest

CTFG

Overall,

- CTR EU536/2014 will mainly harmonise (simplify EU-wide) your way of working, not content of work! Additional study types are adressed as well as special populations

- CTFG is the body for CTs in EU/EEA
  CTFG facilitates and coordinates CT relevant issues, and harmonises positions to CT related topics of interest

CTFG