CLINICAL TRIAL REGULATION AND ETHICS-COMMITTEE PREPAREDNESS

Germany

DIA - Clinical Trial Regulation 2-3 December 2019, AMS

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Conflicts of Interest and Caveat

- ✓ There are no conflicts of interest to declare.
- ✓ The views expressed here do not necessarily represent exactly those of AKEK Germany.

Structure

- Introduction: Current situation in Germany
- Provisions of the CTR
- Implementation of the CTR in Germany
- Registration requirements for ECs
- Responsibilities NCAs / ECs
- Conclusions

Present state of trial approval in Germany

- The German Medicines Act and the GCP-Ordinance implemented the CTD 2001/20/EU in Germany in 2004.
- Assessment of the application dossier independently by MEC and NCA.
- Approval by MEC needed to start a drug trial.
- Only national laws and regulations applicable.
- Option for oral discussions with sponsor.
- Truely independent and autonomous MECs, regulated by state law.

Tasks of Medical Ethics Committees

- **To ensure the protection of the rights, safety and well-being of human subjects involved in a trial *and***
- **To provide public assurance of the protection *by***
- **Reviewing and approving the trial protocol, the suitability of the investigators, facilities, and the methods and material to be used in obtaining informed consent.**

ICH-GCP (E6) and CTD 2001/20/EU Art.2 (k)

CTR 536/2014 Role of Ethics Committees

- **The ethical review shall be performed by an ethics committee (EC) in accordance with the law of the MSc. The review by the EC may encompass aspects addressed in Part I and in Part II as appropriate for each MSc.** (CTR Art. 4)

→ **Contradiction to DoH and ICH-GCP**

→ **In Germany ECs will review Part I and II.**

Application Dossier for Initial Application

- **Part I:** **Trial protocol**, scientific background, risk (harm) – benefit assessment, IB, details specified in Article 6 and Annex I
- **Part II:** **Informed Consent material**, qualification of investigators and suitability of study sites (centres), insurance etc., details specified in Article 7 and Annex I

Part I: Evaluated by all MS concerned, reporting MS coordinates the assessment and provides ‘single decision’.

Part II: Evaluated by all MS concerned, each MS provides **its** decision.

Ethics Committee - Definition

‘an independent body in a Member State established in accordance with national law and empowered to give opinions for the purposes of this Regulation, **taking into account the views of lay-persons, in particular patients or patients organisations’.**

CTR Art.2 2. (11)

THE IMPLEMENTATION LAW

- In November 2016 the German Parliament passed the implementation law for the CTR 536/2014.
- The law speficies the structure and composition of ECs, tasks and responsiblities of the NCAs and the ECs, and their cooperation.

Implementation Law : Registration of MECs

***Requirements** (AMG § 41 neu)*

1. **Documented state of the art expertise of the members,**

2. **Multidisciplinary composition: at least one lawyer, one person with expertise in medical ethics, three practising physicians(one pharmacologist), one biostatistician and one lay person,**

3. **Assured equal access for female and male members to the EC,**

Implementation Law : Registration of ECs

Requirements (§ 41 neu)

5. **By-laws covering internal procedures, transparency, decision-making etc.,**

6. **Business office with adequately qualified staff**,

7. **Adequate technical equipment and performance,**

8. **Proof of the independence of the members and external experts (= no CoI)**

Responsibilities of EC and NCA

- **Part I will be assessed jointly by NCA and EC, NCA taking the lead → lead coordinator.**

- **Part II will be assessed solely by competent EC.**

- **The final decision (Art.8) by the MS Germany will be provided by the competent German NCA, respecting the opinion of the competent EC.**

Further News and Innovations

- About 35 MECs got registered up to now.
- The MECs will be randomly allocated to the approx. 1000 applications/year.
- About 190 applications have been successfully assessed under the conditions and timelines of the CTR.
- Sponsors had occasionaly problems with the 12 calender day limit for responding.
- NCA and MEC will offer scientific and ethical advice before submission.

Germany is well prepared for the CTR 536/2014 and the EU MDR and IVDR.

Further News and General Framework

- The Association of MECs in Germany tries hard to harmonize procedures.
- There is a joint working party with the NCAs.
- Substantial Amendments are treated in the same way as a trial application, → NCA and MEC.
- MECs are involved in the assessment of SUSARs and the annual safety reports.
- The involvement of MECs in the supervision of ongoing trials is not very developed.

Impact of the CTR - Institutionally

- ECs get marginalized
- ECs get dependent to the government
  - registration etc., by-laws
  - loose the right to provide their own statement re Part I and have to col-laborate with the NCA
  - loose their financial autonomy
- The honorary sytem of ECs is at risk, the impact of the individual member weakens.
- The final decision (Art.8) is done by the NCA.

Impact of the CTR - Workwise

- Considerable strain due to very short timelines.
- No more (oral) discussions with the sponsor, communication in writing(foreign language) only.
- Increased affinity to IT-structured workflow needed.
- More communication and probably compromising with NCAs.
- ECs have to be available 365 days/year.

Conclusions

- ✓ Due to the CTR the ECs will loose a considerable part of their independence from the government: The government defines the registration requirements, the tasks and the fees of ECs.
- ✓ Many procedures have been standardized but the scope of the tasks of ECs is now completely up to the Member States – a serious step backwards compared to the CTD 2001/20/EU.

Conclusions

- ✓ In Germany the MECs are responsibly involved in the assessment of Part I AND II.
- ✓ The cooperation between NCA and EC has been tested in about 190 authorisation dossiers under the conditions of the CTR.
- ✓ The Implementation of the CTR is well prepared in Germany.

References

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