CLINICAL TRIAL REGULATION AND ETHICS-COMMITTEE PREPAREDNESS
Germany

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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)
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 specifies the structure and composition of ECs, tasks and responsibilities 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 occasionally problems with the 12 calendar 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.
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 collaborate with the NCA
  - loose their financial autonomy
- The honorary system 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

• Hasford J. The impact of the EU Regulation 536/2014 on the tasks and functioning of ethics committees in Germany. Bundesgesundheitsblatt 2017: 60; 830-835.