Col – Statement and Caveat

• I am an active researcher, member of the European LeukemiaNet, which has been funded by the EU, and of the EU-IMI-Project PROTECT.

• The views expressed here do not necessarily represent exactly those of AMEK Germany.
Aims of the Regulation 536/2014

• To promote clinical research in the EU
• To effectively harmonize the authorization and conduct of clinical trials in the EU
• To simplify procedures
• To strengthen the position of the EU as an excellent and leading location for clinical research and drug development.
Appreciation

- Harmonisation and standardisation of the clinical trial requirements in the EU
- Single submission via EU Portal
- Coordinated multistate assessment
- Introduction of the risk-proportionate approach (→ minimal interventional trial)
- Option for co-sponsors
- Transparency
- IMPs free of charge for the subject
Tasks of 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)
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) 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
Assessment Report: Part I

Multinational studies:

• rMS provides initial assessment report within 26 days from the validation date.
• rMS and MSc jointly perform a coordinated review phase within subsequent 12 days.
Assessment Report: Part I – Challenges for the EC

Multinational studies:

- ECs have to review the application very fast in case rMS needs < 26 days, and to submit requests for additional information.
- The EC of the rMS should provide its own statement already for the initial assessment report.
Assessment Report: Part I – Challenges for the EC

Multinational studies:

→ For all other studies the review phase of 12 days is the only chance to get the MSc ECs point of view integrated.

Mononational studies:

→ The EC should provide its own statement already for the initial assessment report.
Assessment Report: Part I – Challenges for the EC

Multinational studies:

- The draft assessment report has to be reviewed immediately (1 – 2 days).
- Competent (medical, ethical, English) EC-spokesperson needed for the review phase.
- The role and impact of the members of the Ethics Committee get reduced.
- ECs typically work in an honorary capacity only and do meet once or twice a month.
Request for additional Information

Part I

• Only via/by the rMS

• Sponsor has to submit/respond within 12 days, otherwise the application shall be considered as withdrawn in all MSc.

• Extension of assessment period for the assessors (NCA/EC) up to 31 days.
Decision on the Clinical Trial

A MSc shall refuse to approve a clinical trial if it disagrees with Part I of the assessment report of the rMS on any of the grounds referred to in the second subparagraph of paragraph 2 of this Article, or finds, on duly justified grounds, that the aspects listed in Article 7, paragraph 1, are not complied with or where an ethics committee has issued a negative opinion which in accordance with national law is valid for the entire MS.

(Article 8, 4.)
Decision on the Clinical Trial – Challenges for the Ethics Committee

- ECs have to review the final assessment report part I to decide about acceptance and to provide a conclusive written statement within 3 days.

- ECs typically work in an honorary capacity only and do meet once or twice a month.
Tacit Authorisation

If the MSc does not respond within the respites set, the resulting ‘decision’ is in favour of the sponsor.

The concept of ‘tacit authorisation’ pertains to many respites.

What happens if the Ethics Committee does not provide its decision in time?

→ Nonobservance of the DoH?
The ethical review shall be performed by an independent ethics committee (IEC) in accordance with the MS’s national legislation. The review by the IEC may encompass Part I and Part II as appropriate for each MSc.

MS shall ensure that the timelines for the review by the IEC are aligned with the timelines set out in the Regulation.
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’.
How to learn about the views of patients or patients’ organisations about a particular trial given the very short respites?
Conclusions

• Many procedures have been standardized but the scope of the tasks of Ethics Committees is now completely up to the Member States – a serious step backwards compared to the CTD.

• The very rigid communication requirements and short respites may result in increasing numbers of relapses/rejections, and subsequent resubmissions, time delays and costs.

• The very short respites ask for full-time professional Ethics Committees instead of the currently prevailing honorary system.
Conclusions

• The regulation does not clarify how the sponsor learns about the concerns of the MSc in time and how the sponsor can inform the MSc which modifications get accepted to meet the concerns prior to the final decision of the rMS/MSc.

• The request to take the patients’ view into consideration remains a soap-box oratory only, given the very short time allowances.
Conclusions

✓ The Ethics Committees will try hard to meet these challenges.