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on Medical Research Ethics

Commission Guidelines for the implementation of the Clinical Trials Regulation

NTA Ethics

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Background

Based on directive 2001/20/EC of the clinical trials on medicinal products for human use, the Commissions' duty is to draw up and publish:

- **Article 1.3:** The adoption of the principles of good clinical practice
- **Article 8:** Application format and documentation to be submitted in an application for an ethics committee opinion
- **Article 9.8**: Format and contents of the submission of a new CT; submission of the amendment; the declaration of the end of the trial:
- **Article 11.3** Establishment of the European database
- **Article 15**: Master file on the trial, archiving, qualifications of inspectors and inspection procedures
- **Article 18**; Safety reporting

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Current guidelines

Since 2004, COM has issued guidance documents in order to ensure a uniform application of the legislation on clinical trials in Europe. The guidelines specify in particular:

- The information to be submitted to the competent authorities and to the ethics committees – APPLICATION AND APPLICATION FORM
- The requirements on safety monitoring and the reporting of adverse reactions – SAFETY REPORTING
- The specific requirements regarding the products and the clinical trials- QUALITY OF THE IMP
- The inspections of competent authorities and the applicable procedures - INSPECTIONS
- The requirements regarding Good Clinical Practice, including the documentation of the clinical trials, publication of the trial results etc. – ADDITIONAL INFORMATION

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EudraLex - Vol 10 Clinical trials guidelines

- All the guidance documents are put together, in volume 10 of the publications as "The rules governing medicinal products in the European Union" https://ec.europa.eu/health/documents/eudralex/vol-10_en
- The Commission has prepared all these guidelines in consultation with Member States
  - Since 2001 COM has arranged meetings of the *ad hoc* group for the development of implementing guidelines for the "clinical trials directive"; it is nowadays called either *ad hoc* or *expert* group on clinical trials

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- Clinical trials are to be conducted accordance with the Directive and the above guidelines until the new Regulation 536/2014 will become applicable.
- From Commissions webpage http://ec.europa.eu/health/human-use/clinical-trials/ (referred 29.1.2017):
  - The Commission has and will continue to issue guidance documents in order to ensure a uniform application of the legislation on clinical trials in Europe.
  - The recommendations and guidelines further specifying various aspects of clinical trials, are currently being revised and updated to be in line with the requirements of the Clinical Trials Regulation.
  - The guidelines will be launched for public consultation in sets between Q3 and Q4 of 2016. The aim is to finalise and publish them between the end of 2016 and mid-2017.
  - This information will be updated progressively once the new guidelines are prepared.

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Commissions working plan

- The COM presented the draft working plan for ad hoc group in summer 2014. Priority 1 projects are those required by the Clinical Trial Regulation (CTR), namely the
  - Implementing Act on GCP Inspections
  - the Delegated Act on GMP for IMP and
  - the Guidelines on GMP for IMP.
- All remaining guidelines fall under the second priority, e.g.
  - Ethical considerations for the CTs with paediatric population
  - Risk proportionate approach in clinical trials
  - Lay person summary of the results etc.
- Priority 3 projects are those for which the ad hoc group will be only consulted. E.g: the Application form, the Assessment report part I and II and a document outlining the working process for cooperation on safety issues between Member States; these will be decided by Clinical Trials Facilitation Group (CTFG) in consultation with the ad hoc group.

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- There is no legal basis in the Regulation for some of the current guidelines e.g.
  - Guidance on the request for authorisation and the application for EC opinion
  - List of data fields contained in the ”EudraCT” to be made public
- New guidelines are being prepared by EMA and its’ expert groups on the entries of the EU Portal and Database.
- Application dossier is defined in the legislation (Annex I)
- COM has stated that **Q&A document** will be a "living" document with further Q&As being added and updated as necessary. For example, differences between the Directive and Regulation may also be included in the document.
- *Transition period* has been one of the major issues in drafting the Q&A document. Other issues are e.g. defining the end of the trial; guidance on cluster randomized trials, timing for the input of the results from the sub-studies; etc.

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ANNEX I Application dossier for the initial application – to assess Part II

- K. RECRUITMENT ARRANGEMENTS (INFORMATION PER MEMBER STATE CONCERNED)
- L. SUBJECT INFORMATION, INFORMED CONSENT FORM AND INFORMED CONSENT PROCEDURE (INFORMATION PER MEMBER STATE CONCERNED)
- M. SUITABILITY OF THE INVESTIGATOR (INFORMATION PER MEMBER STATE CONCERNED)
- N. SUITABILITY OF THE FACILITIES (INFORMATION PER MEMBER STATE CONCERNED)
- O. PROOF OF INSURANCE COVER OR INDEMNIFICATION (INFORMATION PER MEMBER STATE CONCERNED)
- P. FINANCIAL AND OTHER ARRANGEMENTS (INFORMATION PER MEMBER STATE CONCERNED)
- Q. PROOF OF PAYMENT OF FEE (INFORMATION PER MEMBER STATE CONCERNED)
- R. PROOF THAT DATA WILL BE PROCESSED IN COMPLIANCE WITH UNION LAW ON DATA PROTECTION (***NOTE: NEW REGULATION ON DATA PROTECTION (679/2016) LEAVES ROOM FOR NATIONAL MANOEUVRE***)

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- In the latest expert group meeting (26th Jan 2017) COM suggested that MSs should co-operate in harmonizing the application dossier related to PART II evaluation.
- EU does not have any power at all to determine the tasks of EC, all the responsibilities lay with the MS.
- The sub-group for drafting the Assessment report II volunteered this task

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Conclusions

- From a formal point of view COM and EMA are in charge of conducting the implementation on CTR, including drafting the implementation guidelines on the CTR
- There should not be as much room for national interpretations as there has been in Directive
- Aspects covered by Part II are exceptions to that