Clinical Trial Facilitation Group
CTFG

HMA
Heads of Medicines Agencies

Update on EU member state harmonisation

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Clinical trials facilitation group (CTFG)

- Established by Heads of Medicines Agencies in 2004 to coordinate the implementation of the EU clinical trials Directive 2001/20 EC across the member states
- CTFG acts as a forum for discussion to agree on common principles and processes to be applied throughout the European medicines regulatory network (EMRN)
- It **promotes harmonisation** across the national competent authorities (NCAs)
  - Clinical trial applications, substantial amendments
  - Safety assessment (Development Safety Update Reports & urgent safety issues)
  - Development of guidelines e.g. contraception, Reference Safety Information, GLP
  - Development of assessor training (supported by the EU Network Training Centre)
- Final decisions on applications are made by the individual NCAs and ethics committees

Implementation of the Clinical Trials Directive 2001/20/EC Harmonization has not been achieved

Fragmentation of the authorisation regime

- Clinical Trials are assessed by several National Competent Authorities (**NCAs**) **independently**
- Independent assessment by ethics committees

Lack of harmonization

- National laws
- Different interpretation of the CT directive/guidelines
- Different approach to assessment

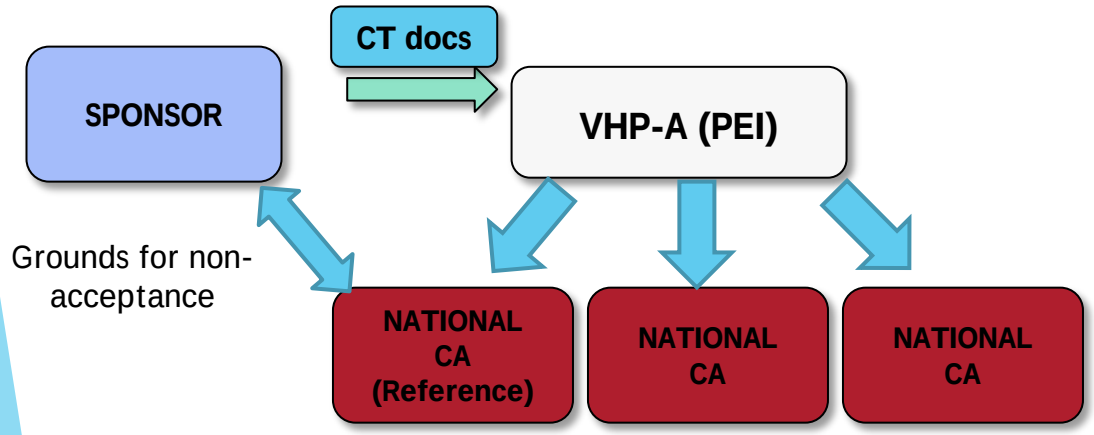
→ Divergent decisions for the same clinical trial

- Only 25% of EU CT applications between 2005 – 2016 were multinational
- Clinical trial applications fell each year between 2007 - 2014

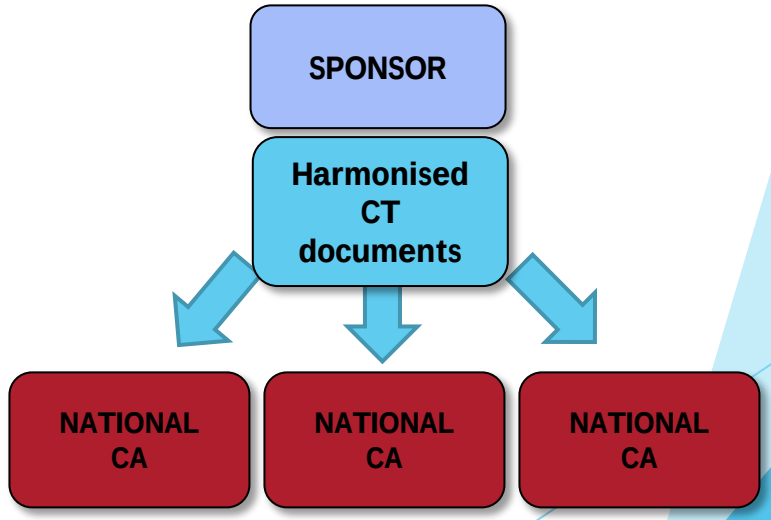
Voluntary Harmonisation Procedure

- CTFG has set up a European-wide application procedure for multinational trials under the Directive 2001/20/EC (administrated by the Paul Ehrlich Institute)
- Assessment of **clinical trial applications & substantial amendments** is led by a 'reference NCA'

VHP - step 1:
Submission & assessment (60 days)



VHP- step 2
National submission (≤10 days)



VHP-A – VHP administrator (VHP-CTFG@VHP-CTFG.eu)

Voluntary harmonisation procedure

- Approximately 20% of multinational clinical trial applications in EEA are VHPs
  - Over 1000 CT applications have been submitted through VHP
- Twenty six EEA NCAs are currently participating in VHP
- Some member states offer the involvement of Ethics Committees in a VHP ("**VHP plus"**)
- This involves only the assessment of the submitted documents on the benefit/risk, **investigators brochure and study protocol**
- A list of the NCAs that involve ethics committees and the specific conditions to do so is available on the CTFG website
- http://www.hma.eu/fileadmin/dateien/Human_Medicines/01-About_HMA/Working_Groups/CTFG/2017_01_CTFG_VHP-Plus_List_of_participating_National_Competent_Authorities.pdf

EU CT Regulation 536/2014

- VHP is providing valuable experience for NCAs for the new CT Regulation
- An assessment report is required for each CT application & substantial modification
  - A template multinational part I assessment report was agreed at CTFG in 2016
    - Detailed report tailored to the requirements of the new Regulation with quality, preclinical, clinical, regulatory and statistical sections
    - This template is currently being used
  - Under the Regulation, the final Assessment Report will be published
- Article 98 Transitional Provision
  - CTs approved under the Directive can continue for 3 years under the Directive after implementation of the Reg. **Transition will be required** for trials that are ongoing after this
  - Transition of VHPs will be easiest
    - **VHPs will already have a part I Assessment Report and Reporting Member State**
    - **VHP submissions will be no longer be accepted when the Regulation is implemented**

EU Reg. 536/2014: Key improvements

The objective of the new CT Regulation is to create an environment that is favourable for conducting clinical trials in Europe:

- Single submission of a single set of documents, through EU portal
- Strict timelines for assessment
  - CT applications: Part I and Part II conclusions **within 45 days from validation date** (+31 days if there are requests for further information)
  - Substantial modifications: 38 days from validation date
- Coordinated assessment of common documents in multinational CTs
  - Protocol, Investigator's Brochure, IMPD assessment led by reporting member state
- Single decision per member state (NCA + Ethics) 5 days after completion of Part I & Part II

EU CT Regulation 536/2014: Cooperation in safety assessment

- Article 44 states that member states shall cooperate in the assessment of clinical trial safety data
  - CTFG has arranged worksharing of assessment of DSURs for multinational trials/IMPs across NCAs (coordinated by SUKL)
  - Template Assessment Report developed and agreed
  - Lead NCA conducts assessment ("safety assessment member state")
    - Draft AR generated
    - Other Member states have an opportunity to comment/raise considerations
    - saMS communicates with sponsor
    - All member states concerned may follow up with actions
  - CTFG is working with EMA & stakeholders to functional requirements of IT system to support cooperation

Training

- Assessor training seminars/workshops have been EU Network Training Centre, jointly supported by the Heads of Medicines Agencies and the European Medicines Agency
- Aim of the training sessions is to improve harmonisation

Recently Completed:

- EU CT Regulation training, EMA (MHRA & AEMPS, March 2016)
- CT Safety training & workshop, Dublin (HPRA, September 2016)
- CT clinical assessor training, Rome (AIFA, November 2016)

Planned:

- First in Human training, EMA (FAMHP, March 2017)
- CT Safety training & workshop, Prague (SUKL, October 2017)
- CT Quality assessor training (to be decided)

Thank you

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