SETTING UP INTERNATIONAL CLINICAL TRIALS IN EUROPE: THE EORTC EXPERIENCE

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European Organization for Research and Treatment of Cancer

EORTC (European Organization for Research and Treatment of Cancer)

EORTC

- Not for profit research organization
- Main mission: promote and conduct research to improve cancer care
- To decrease the time needed to evaluate new therapeutic modalities
- To disseminate state-of-the-art knowledge with the final goal of improving the standard of cancer care
- To interact with health policy makers to promote clinical research

EORTC

- **Core activity: conduct clinical trials :**

  → Multidisciplinary and multinational efforts (investigator network: more than 200 institutions from 31 different countries; +/- 2,000 collaborators)

- **More than 5,000 patients are entered into EORTC trials each year (database of more than 140,000 patients)**
- **30,000 patients being followed-up**
- **More than 100 trials ongoing**

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EUROPEAN DIRECTIVE 2001/20/EC (CTD): HURDLES TO BE TAKEN & PRACTICAL APPROACH

CTD: hurdles to be taken & practical approach

Results of the implementation:

- **Substantial increase in complexity at the level of documentation that needs to be submitted to both CA and ECs (increased administrative requirements)**
  - **Resources for staff needed (→ cost implications)**
  - **Take time to adequately prepare paperwork (→ to avoid delays by non validation)**
  - **Take also into account the extensive safety reporting requirements**

CTD: hurdles to be taken & practical approach

- **It's clear by now that there is no real harmonization of administrative provisions governing clinical trials!**
  - **Additional national requirements**
  - → **Be prepared for language problems!**
  - → **General lack of clarity as to what national requirements are**
  - → **Experience has shown that national requirements may change over time - certain may disappear while others may be introduced**
  - → **EudraCT number not only reference: always quote national number on additional correspondence**
  - → **For multi country trials, the cumulative effect of additional national requirements becomes very cumbersome!**

CTD: hurdles to be taken & practical approach

- **Different outcome of review in multinational trials**
  - **Protocol changes requested by 1 competent authority can lead to protocol amendments to be made across Europe**
  - **Try to reason first with CAs, propose alternative solutions**

- **Difference in opinion/interpretation across Member States in definitions:**
  - **Substantial and non-substantial amendments**
  - **IMPs/NIMPs**
    - **Member States have taken inconsistent approach to the designation of background and "standard of care" therapies used in multi-country clinical trials, leading to the same product in the same trial being listed as an IMP in one Member State but not in another**

CTD: hurdles to be taken & practical approach

- **Difficulties with ECs:**
  - **Implementation of the single EC- opinion procedure is complex!**
    - **Implementation at the national level results in divergent regulation and practice**
    - **This generates problems such as longer procedures, local ECs have to respond to central EC within given timelines leading to delays or local sites not being covered by the central EC opinion, confusion over role of local and central EC,…**
  - **Parallel submission foreseen in the guidelines sometimes not possible**
  - **No clear communication between ECs and CAs**
  - **Fees: write waiver letters**

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Additional obstacles related to noncommercial trials

Additional obstacles related to non-commercial trials

- **One size doesn't fit all: the CTD did not consider the different categories of clinical research performed by the commercial vs. non-commercial sponsors: similar rules and requirements for both commercial and non-commercial studies led to major obstacles to academic research**
- **Sponsorship: Multi-national non-commercial trials are difficult to organize in an efficient way if sponsor is based at an academic institution**
- **IMPs have to be made available by the sponsor free of charge! (but no clear definition of IMPs/NIMPs)**

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Conclusion

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- **Running large international clinical trials more difficult than ever !**
  - **Be prepared**
  - **Needs professional and multifactorial approach**
  - **Document everything very well**
  - **Seize every opportunity to address these fundamental issues in order to improve the current regulatory environment**
- **The disharmony and difficulties encountered may affect the competitiveness and attractiveness of clinical research in the EU**

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- **Harmonization of implementation of the Clinical Trials Directive and the removal of unnecessary bureaucracy would benefit health care providers and patients by increasing the development and access to innovative medicines and optimal therapeutic strategies**

  → **Although the cultural, ethical, linguistic differences have to be respected, there's room for improvement**