The Road Map Initiative for Clinical Research in Europe

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Background of Roadmap Initiative

Reason:

- 2001: new CT-directive
- EU-representatives have only little insight in the situation of IITs.
- only minor influence by academical, independent researchers
- Negative effect for independent research
- Lobby work is essential

Background of Roadmap Initiative

October 2008:
CLINT invited different EU-funded projects, doing research in the area of CT directive (CTD) or clinical trials.

Background of Roadmap Initiative

Members:

CLINT: Facilitating international prospective clinical trials in stem cell transplantation (EU project)

EBMT: European Group for Blood and Marrow Transplantation

ECRIN: European Clinical Research Infrastructures Network

EFGCP: European Forum for Good Clinical Practice

ELN: European Leukaemia Net (EU project)

ICREL: Impact on Clinical Research of European Legislation (EU project)

EORTC: European Organisation for Research and Treatment of Cancer

UCLAN: University of Central Lancashire, Centre for Professional Ethics

Goals of Roadmap Initiative

Goals:

- Represent independet researchers
- Buildung up a strong voice to be heard at the EC
- Joint recommendation on specific topics regarding CTD
- Include representatives from different stakeholder groups
- Participating in CTD Review:
  Towards an improvement for academical researchers

Action plan of Roadmap Initiative

1. Several „Set-up meetings“ in 2009
2. Publicity
   - Editorial in British Medical Journal*
3. Joint recommendation
   - Topics
   - 5 Workshops in 2009 and 2010
   - Survey on level of consensus (EFGCP)
   - Final workshop with EU and stakeholders

* Frewer et al., BMJ. 2010 Apr 9;340:c1862. doi: 10.1136/bmj.c1862.
Has the European Clinical Trials Directive been a success?

Action plan of Roadmap Initiative

Date	Venue	Topic	Organised by
7th July 2009	Brussels	Single Clinical Trial Approval (CTA) Process	EFGCP
21st Sept 2009	London	Co-Sponsorship and contractual issues	CLINT/EBMT
18th - 19th Jan 2010	Paris	Risk-based approach and Ethics committees	ECRIN
8th Feb 2010	Brussels	Pharmacovigilance	EORTC
17th Mar 2010	Brussels	Stakeholder conference with EU – Final Workshop	EFGCP

Results: Single CTA Workshop

Clinical trial application (CTA) ☞ Work Overload

Multiple versions of

- application forms and
- application dossiers
- and divergent opinions

Main recommendation from academia:

- One approval process
- one single dossier, mainly english
- No additional requirements
- Specified timeline across Europe Union

Further recommendation from academia:

- More funding or reducing administrative costs

Results: Co-Sponsorship Workshop

One Sponsor ☞ International responsibility

- For academia nearly impossible

Main recommendation/conclusion from academia:

- Clearer definition of co-sponsoring
- Co-Sponsoring options
  - geographical delegation e.g. 1 co-sponsor per country
  - special clinical trial tasks delegation
  - Model contracts are available (Health dep. UK)

Results: Risk-based approach Workshop

Academical trials ☞ No difference between trials in the frame of market authorisation and in the frame of optimum-use trials

Conclusion:

- Need to downgrade regulations
- Definition („prefinal“) of
  - risk
  - risk-categories in clinical trials
  - 9 relevant areas
  - Risk-based adaption of requirements (basis)
- Development of guidance and procedures

Results: Risk-based approach Workshop

ELN European LeukemiaNet

Proposal for adapted requirements

TABLE 1

Clinical trials on medicinal products: proposed adaptations of requirements for each process based on participant's risk categories

Process	Category 1 (without MA)	Category 2 (with MA, new indication/population / condition)	Category 3 (with MA, licensed indication/population/ condition)
Ethical review	Full review	Full review	Light patient information Expedited review
Competent authority	Clinical Trial Authorisation	Clinical Trial Authorisation	Notification
Safety reporting	All SUSARs on this product reported to EudraVigilance and to the NCA of the sponsor + Periodic Safety Report to Ethics Committees and investigators	Only SUSARs from this trial from EudraVigilance to the NCA of the sponsor + Periodic Safety Report on this trial to ethics committees and investigators	SUSARs sent to EudraVigilance CTM, no expedited SUSAR reporting + Periodic Safety Report on this trial to NCA, ethics committees and investigators
Monitoring* (also takes into account the hazard to data integrity)	Decision tree for risk definition, and adapted monitoring strategy	Decision tree for risk definition, and adapted monitoring strategy	Decision tree for risk definition, and adapted monitoring strategy

Results: Risk-based approach Workshop

Sponsor	Yes (flexible arrangements to share responsibility)	Yes (flexible arrangements to share responsibility)	Yes (flexible arrangements to share responsibility)
Insurance	No-fault insurance by sponsor. Explore coverage by health care system or insurance packages	Explore coverage by public health care systems.	Explore coverage by public health care systems. No insurance required for "minimal risk" category
Labelling*	Current requirements apply but review critically Annex 13 whether there is room for facilitation	Simplified labelling ? or other traceability procedure ?	Simplified labelling ? (CTD Art 14+annex13) Or no specific labelling ? or other traceability procedure ?
Documentation*	IMPD	IMPD = harmonised SmPC + quality / safety data Cross-reference to other IMPD Facilitate definition and access to suitable SmPC	IMPD = harmonised SmPC Cross-reference to other IMPD 5-years retention of TMF if no MA application Facilitate definition and access to suitable SmPC
Inspections	Current practice	Medium priority. Adapt inspection to risk definition in protocol	Low priority. Adapt inspection intensity to procedural risk as defined in protocol

* Flexibility already possible under the current legislation

Results: Ethics committees Workshop

Academical trials ☞ Work/Administrative overload

- Multiple application dossiers for MS and national countries
- Different languages
- Different opinions

Main recommendations:

- Harmonisation: Training for responsible EC members
- Specified timelines across Europe Union
- Common application dossier for CA and REC (in all MS)
- Single EC opinion, but national input (e.g. informed consent and site assessment)
- Risk-based approach, risk-level defined by sponsor – approved by REC

Results: Pharmacovigilance

Different and more regularities and timelines ☞ patient safety questionnable

Main recommendations:

Simplified and harmonised SUSAR reporting process:

- No expedited reporting to ECs and PIs. They should receive annual safety reports (ASR) with risk/benefit analysis and line listing of SUSARs and SARs.
- The role of DSMBs should be strengthened

Results: Information on ELN Web

- All reports available at www.leukemia-net.org > International Trials > Workshops > Roadmap Initiative

  http://www.leukemia-net.org/content/international_trials/workshops/the_road_map_initiative

News from the EC

- ENTR/CT1: …guidance for the request for authorisation of a CT to the competent authority…
  - New: application form (nov. 2009)
  - Substantial Amendment Notification Form (june 2010)
  - Declaration of the End of Trial Form (june 2010)
- Guidance documents applying to CT (Q&A) (sep 2010)

  http://ec.europa.eu/health/documents/eudralex/vol-10/index_en.htm
- AE-Guidline for revision (CT3)

Links will be placed on ELN website