Patients' perspective on the EU Clinical Trials Directive

ELN Workshop, 1 February 2011

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Leukämie online.de

LeukaNET
Leukemia Advocates Network

Well-frequented leukemia patient community in the German speaking web

EUROPEAN CANCER PATIENT COALITION

Umbrella for 315 cancer patient organisations in 42 countries

CML AdvocatesNetwork

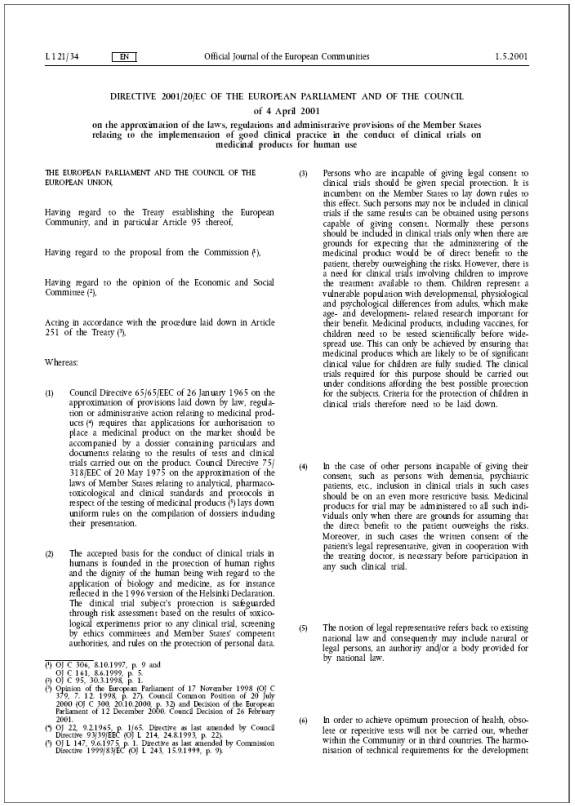
Network of 53 leukemia patient groups in 43 countries

iCMLf International Chronic Myeloid Leukemia Foundation

Patient in scientific advisory committee & in staff

EU Regulation of Clinical Trials

- Clinical Trial Directives 2001/20/EC and 2005/28/EC **introduced to protect us:**
  - **Ensure safety** of participants
  - **Guarantee rights** of participants
  - Harmonisation of trial procedures across the EU
  - Increase reliability and robustness of trial data



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DIRECTIVE 2001/20/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 4 April 2001
on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 95 thereof,

Having regard to the proposal from the Commission (1),

Having regard to the opinion of the Economic and Social Committee (2),

Acting in accordance with the procedure laid down in Article 251 of the Treaty (3),

Whereas:

(1) Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products (4) requires that applications for authorisation to place a medicinal product on the market should be accompanied by a dossier containing particulars and documents relating to the results of tests and clinical trials carried out on the product. Council Directive 75/318/EEC of 20 May 1975 on the approximation of the laws of Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of medicinal products (5) lays down uniform rules on the compilation of dossiers including their presentation.

(2) The accepted basis for the conduct of clinical trials in humans is founded in the protection of human rights and the dignity of the human being with regard to the application of biology and medicine, as for instance reflected in the 1996 version of the Helsinki Declaration. The clinical trial subject's protection is safeguarded through risk assessment based on the results of toxicological experiments prior to any clinical trial, screening by ethics committees and Member States' competent authorities, and rules on the protection of personal data.

(3) Persons who are incapable of giving legal consent to clinical trials should be given special protection. It is incumbent on the Member States to lay down rules to this effect. Such persons may not be included in clinical trials if the same results can be obtained using persons capable of giving consent. Normally these persons should be included in clinical trials only when there are grounds for expecting that the administering of the medicinal product would be of direct benefit to the patient, thereby outweighing the risks. However, there is a need for clinical trials involving children to improve the treatment available to them. Children represent a vulnerable population with developmental, physiological and psychological differences from adults, which make age- and development- related research important for their benefit. Medicinal products, including vaccines, for children need to be tested scientifically before widespread use. This can only be achieved by ensuring that medicinal products which are likely to be of significant clinical value for children are fully studied. The clinical trials required for this purpose should be carried out under conditions affording the best possible protection for the subjects. Criteria for the protection of children in clinical trials therefore need to be laid down.

(4) In the case of other persons incapable of giving their consent, such as persons with dementia, psychiatric patients, etc., inclusion in clinical trials in such cases should be on an even more restrictive basis. Medicinal products for trial may be administered to all such individuals only when there are grounds for assuming that the direct benefit to the patient outweighs the risks. Moreover, in such cases the written consent of the patient's legal representative, given in cooperation with the treating doctor, is necessary before participation in any such clinical trial.

(5) The notion of legal representative refers back to existing national law and consequently may include natural or legal persons, an authority and/or a body provided for by national law.

(6) In order to achieve optimum protection of health, obsolete or repetitive tests will not be carried out, whether within the Community or in third countries. The harmonisation of technical requirements for the development

(1) OJ C 306, 8.10.1997, p. 9 and OJ C 141, 8.6.1999, p. 5.
(2) OJ C 95, 30.3.1998, p. 1.
(3) Opinion of the European Parliament of 17 November 1998 (OJ C 379, 7. 12. 1998, p. 27), Council Common Position of 29 July 2000 (OJ C 300, 20.10.2000, p. 32) and Decision of the European Parliament of 12 December 2000. Council Decision of 26 February 2001.
(4) OJ 22, 9.2.1965, p. 1/65. Directive as last amended by Council Directive 93/39/EEC (OJ L 214, 24.8.1993, p. 22).
(5) OJ L 147, 9.6.1975, p. 1. Directive as last amended by Commission Directive 1999/83/EC (OJ L 243, 15.9.1999, p. 9).

- Implementation does **not serve the interests of patients** (nor research nor industry):
  false promises of safety through bureaucracy

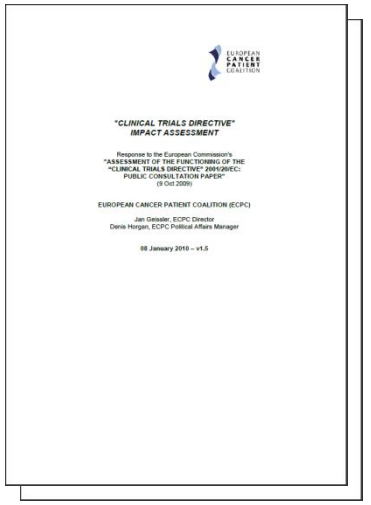
Suggestions for modification of CTD: Perspective from the patients

- **Reverse the trend** from academic to industry-led cancer research and reduced numbers of trial sites
- **Return to a research-friendly framework** in Europe
  - **Consider risk-adapted approaches** (e.g. therapy optimization)
  - **Safety reporting** adjusted to real need
  - **Re-consider applicability of CTD** to non-drug trials (eg SCT)
  - Increase transparency of **public information about trials**
  - Re-assessment of cost/benefit of **new insurance requirements,** especially to support long-term observational studies in oncology
- **Inclusion of patient groups** when 'needs for protection' are discussed – in policy but also ethics reviews

What we patients have done about the CTD: Nothing about us without us…

- **Worked with clinicans to understand CTD's impact on investigator-led research** (ELN, Kompetenznetze)
- **Shared positions** with professional associations & working groups (EHA, EFGCP, ELN, etc)
- **"Lobbied" the EU Commission and EU Parliament**
- **Patients' voice speaking at conferences (DIA, EFGCP)** to increase public pressure

Patient groups proactively address the CTD on EU level



- **EU Stakeholder consultation meetings** (09-2009) and individual meetings with Pharma Unit in DG Sanco
- **Participation in EU Public Consultation** (01-2010), ECPC, European Patients' Forum
- Influence in **EMA's** "Patient & Consumer Working Party"
- Board Membership in **European Forum for Good Clinical Practice** (EFGCP)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EF GCP

Some examples on CTD impact in hematology that we have used

- Adult and pediatric ALL trials - CTD has reduced participation rates significantly
- Low grade lymphoma (2007, OSHO 70 study) - protocol approval process took **four times longer and costs trial approval rose by tenfold**
- German Hodgkin Study group: **100.000 copied pages** submitted for a single study with 280 participating clinics and 65 ethics committees.
- **Patients with co-morbidities or older patients** more often excluded from clinical trials

Next steps – joined forces?

- **Long term** – requires long breath
  - New legislative proposal (2012 EU Commission → EU Parliament)
  - Political pressure to accelerate!
- **Short term** – requires coordinated action **now**
  - Implementation on member state level
  - Political pressure to improve practical implementation

- Well coordinated efforts required across diseases and organisations
- **The patients voice can break up deadlocked positions** and help to get away from technicalities

Joining forces to get better answers to cancer patients more quickly.

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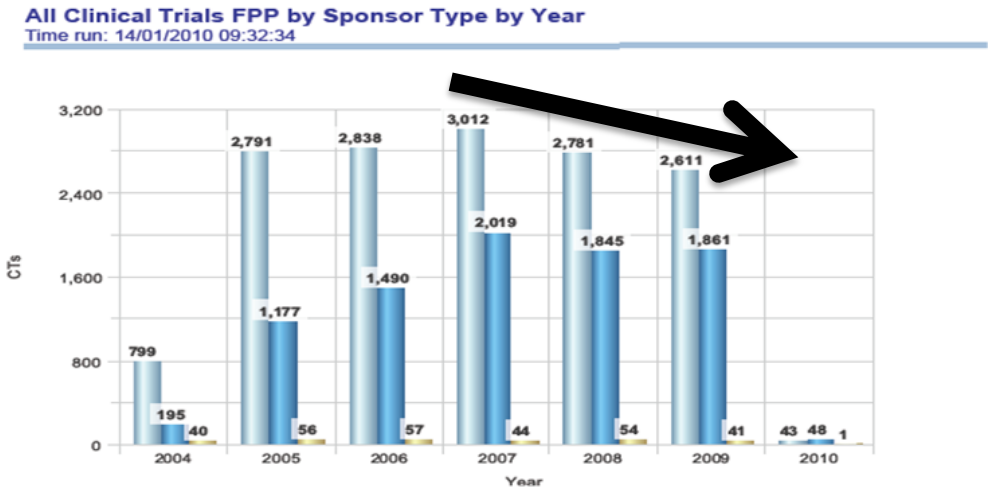
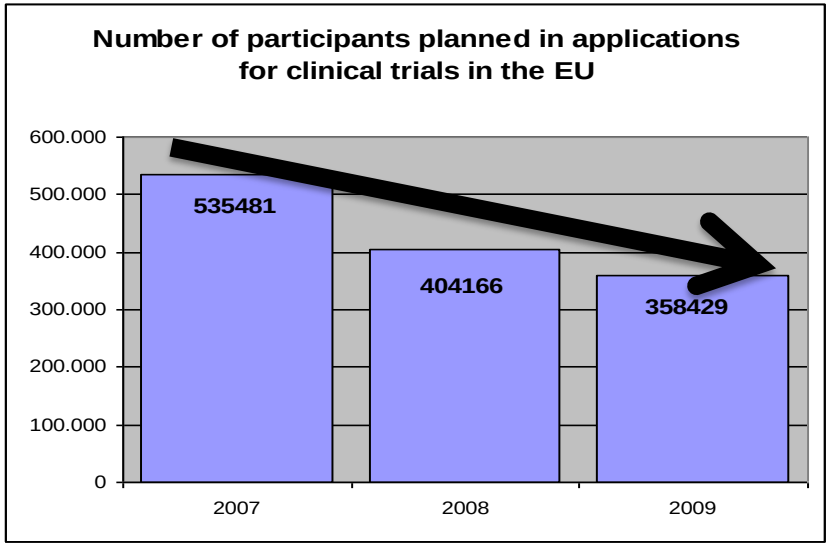
CTD led to a steep decline in # of CTs and patient recruitment



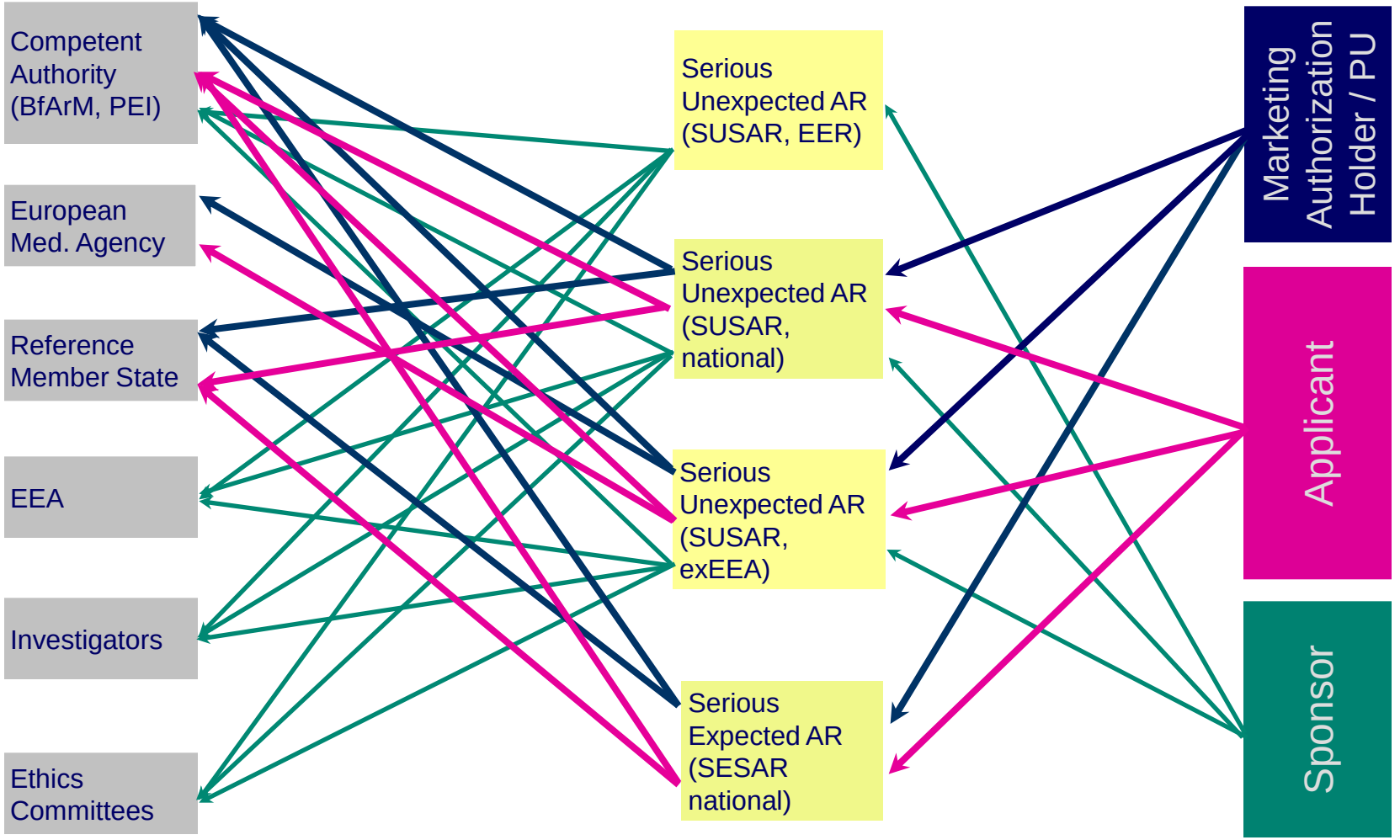
Sponsor Type	2004	2005	2006	2007	2008	2009	2010	CTs Total
Commercial	799	2,791	2,838	3,012	2,781	2,611	43	14,875
Non-Commercial	195	1,177	1,490	2,019	1,845	1,861	48	8,635
	40	56	57	44	54	41	1	293
Grand Total	1,034	4,024	4,385	5,075	4,680	4,513	92	23,803



(Source: ICREL Report 2008)

Example Safety Reporting

Obligatory reporting of unexpected adverse events, based on German implementation of CTD in medicines law (§63b AMG) and Good Clinical Practice act (§13 GCP)



(Source: Paul-Ehrlich Institute 2009)