



Conference on the

Impact on Clinical  
Research of European  
Legislation – ICREL:  
Results & Discussion

2 December 2008

Diamant Centre, Brussels, Belgium



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### Programme Committee

Gonzalo Calvo	Hospital Clinic I Provincial Barcelona, Spain
Xavier Carné	Hospital Clinic I Provincial Barcelona, Spain
Jacques Demotes	French Institute of Health and Medical Research (INSERM) / European Clinical Research Infrastructures Network (ECRIN), France
Christiane Druml	Ethics Committee of the Medical University of Vienna, Austria
Corinne Gaillard	European Forum for Good Clinical Practice (EFGCP), Belgium
Raquel Hernandez	Hospital Clinic I Provincial Barcelona, Spain
Ingrid Klingmann	European Forum for Good Clinical Practice (EFGCP), Belgium
Christine Kubiak	French Institute of Health and Medical Research (INSERM) / European Clinical Research Infrastructures Network (ECRIN), France
Denis Lacombe	European Organisation for Research and Treatment of Cancer (EORTC), Belgium
Stéphane Lejeune	European Organisation for Research and Treatment of Cancer (EORTC), Belgium
Johannes Pleiner	Ethics Committee of the Medical University of Vienna, Austria
Nuria Sanz	Hospital Clinic I Provincial Barcelona, Spain
Diane van Vyve	European Organisation for Research and Treatment of Cancer (EORTC), Belgium

### Faculty

Chantal Bélorgey	Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS), France
Gonzalo Calvo	Hospital Clinic I Provincial Barcelona, Spain
Willy De Greef	EuropaBio, Belgium
Jacques Demotes	French Institute of Health and Medical Research (INSERM) / European Clinical Research Infrastructures Network (ECRIN), France
Christiane Druml	Ethics Committee of the Medical University of Vienna, Austria
Mats Ericson	EFPIA / Wyeth Research, France
Stefan Führung	DG Enterprise, European Commission
Liselotte Hoejgaard	European Science Foundation (ESF), France
Alastair Kent	Genetic Interest Group (GIG), United Kingdom
Ingrid Klingmann	European Forum for Good Clinical Practice (EFGCP) / <i>ICREL Project Coordinator</i> Belgium
Christine Kubiak	French Institute of Health and Medical Research (INSERM) / European Clinical Research Infrastructures Network (ECRIN), France
Denis Lacombe	European Organisation for Research and Treatment of Cancer (EORTC), Belgium
Françoise Meunier	European Organisation for Research and Treatment of Cancer (EORTC), Belgium
Detlef Niese	Novartis, Switzerland
Johannes Pleiner	Ethics Committee of the Medical University of Vienna, Austria



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Bruno Scherrer	Biostatistician Consultant, France
Cees Smit	European Genetic Alliances' Network (EGAN) / Dutch Genetic Alliance (VSOP), The Netherlands
Thomas Sudhop	Federal Institute of Drugs and Medical Devices (BfArM), Germany
Fergus Sweeney	European Medicines Agency (EMA)
Frank Wells	Cambridgeshire 4 Research Ethics Committee, United Kingdom / European Forum for Good Clinical Practice (EFGCP), Belgium
Diane van Vyve	European Organisation for Research and Treatment of Cancer (EORTC), Belgium

### Conference Language

The language of the Conference will be English.

### Conference Rationale

The European Union Clinical Trials Directive 2001/20/EC (EU CTD) was released with the objective of harmonising the regulatory systems, of improving the protection of study participants, of optimising the use of safety information, of ensuring the quality of studies and the credibility of data. As a consequence, the Directive 2001/20/EC<sup>i</sup> was adopted on April 4<sup>th</sup>, 2001 and to be implemented by all Member States on May 1, 2004 (in fact, transposition into national legislation entered into force between 2004 and 2006 in the various EU member states). Rather surprisingly, and due to the role assigned to the European Union (facilitating circulation of products and services, whereas health and ethics remain areas of national policy), this Directive was prepared by DG Enterprise and Industry, and its scope is restricted to clinical trials on medicinal products, an area of major challenge for the industry. This new EU legislation increased the responsibility of clinical trial sponsors and decreased that of the investigators; it led to shared responsibilities between ethics committees and competent authorities, and improved the patients' protection<sup>ii</sup>. A single sponsor in the EU, covered by liability insurance for study-related harm to study participants, has now to submit a clinical trial authorisation application to the national competent authority, and in parallel a request for a single favourable opinion to Ethics Committee(s). With the EU CTD, an EMA-located database for study identification (EudraCT) was implemented and a section for clinical trials added to the EudraVigilance database.

Through harmonisation of the regulatory framework of clinical research, the EU CTD was expected to foster multinational collaboration, to make European clinical science more competitive and the European Union more attractive for industry-sponsored clinical trials. However, many stakeholders now have the feeling that, due to application of the same rules to all types of drug trials and divergent transposition of the Directive's principles into pre-existing national legislations, the Directive partly missed its facilitation and harmonisation targets. In addition, the Directive is considered to impose unnecessary administrative burden and costs which is especially problematic for investigator-initiated clinical research. Therefore industry and academic stakeholders frequently claim (not exactly for the same reasons) for changes in the EU regulatory framework for clinical research<sup>iii</sup>.

The European Commission (DG Enterprise and Industry) and the European Medicines Agency organised a conference in October 2007 to discuss the possible changes to be brought to the Directive. Simultaneously, the DG Research funded, through the health priority of the FP7 cooperation programme, the ICREL (Impact on Clinical Research of European Legislation) project to provide metrics and thus objective arguments for the need to adapt the current legislation with the objective of making clinical research more competitive in the European Union whilst providing fair and equivalent protection to participants in every category of clinical



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research. ECRIN, EORTC, the Hospital Clínic I of Barcelona and the Ethics Committee of the Medical University of Vienna are collaborating in this project coordinated by EFGCP ([www.efgcp.be/ICREL](http://www.efgcp.be/ICREL)).

ICREL collects:

- information on positive and negative impact factors on clinical trials with medicinal products and on other types of clinical research
- figures on the impact of the legislation on the clinical research activity of big Pharma Industry -, SME-, academia-sponsored trials
- data on the resource, cost and effectiveness implication of the CTD implementation for all stakeholders
- comparison of the success of national CTD implementation
- consolidated conclusions on the findings amongst the stakeholders

As data from individual countries, based on different methodologies, suggest that the impact of the CTD may vary from one country to another<sup>iv</sup>, the collection of data throughout the European Union, with the same methodology, will certainly help further describe and interpret this impact.

ICREL's methodology includes the collection, comparison and interpretation of figures from all EU member states on all types of clinical trials on medicinal products sponsored by pharmaceutical companies, biotechnology, SMEs, and academic institutions, on other categories of clinical research, as well as on the impact on ethics committees, competent authorities, clinical research infrastructure, and on the workload, cost and funding of clinical trials. It will compare the situation before (2003) and after (2007) the implementation of Directive 2001/20/EC. Detailed data were obtained through a series of questionnaires (see [www.eortc.be/ICREL](http://www.eortc.be/ICREL)) targeting the different stakeholders: commercial and non-commercial sponsors, ethics committees and competent authorities.

This work will be presented and discussed during the Conference held in Brussels on December 2<sup>nd</sup>, 2008. The resulting discussion and interpretation is expected to help improving Europe's attractiveness and competitiveness for clinical research by delivering the facts for proposing pathways for improvement of the clinical trial environment in the EU, allowing to better balance a high level of patient protection, optimal use of safety information, high quality and credibility of data, with acceptable cost and workload for investigators, sponsors, ethics committees and competent authorities, for both national and multinational studies in the EU.

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<sup>i</sup> 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. OJEC 1.5.2001, L 121/34-44

<sup>ii</sup> Editorial: Who is afraid of the European clinical trials Directive. *Lancet* 361:2167, 2003.

<sup>iii</sup> Druml C, Singer EA, Wolzt M. Report of the 1st meeting of the "Vienna Initiative to Save European Academic Research (VISEAR)" *Wien Klin Wochenschr.* 2006 Apr;118(5-6):Suppl 1-12

<sup>iv</sup> Berendt L, Hakanson C, Friis Bach K, Dalhoff K et al. Effect of European Clinical Trial Directive on academic drug trials in Denmark: retrospective study of applications to the Danish Medicines Agency, 1993-2006. *BMJ*, 336:33-35, 2008.

Agenzia Italiana del Farmaco. Bulletin on Clinical trials of drugs in Italy, 2007. <http://oss-sper-clin.agenziafarmaco.it>

Courcier S, Sibenaler C, Couderc M, Trinquet F, Plétan Y, Lassalle C, La France est un pays attractif pour la recherche clinique : enquête 2006 du LEEM. *Thérapie*, 61:407-418, 2006.

# Agenda

- 07:15 Registration and Welcome Coffee
- 08:00 Welcome and Introduction to the Conference  
*Ingrid Klingmann, EFGCP, ICREL Project Coordinator, Belgium*  
*Jacques Demotes, INSERM / ECRIN, France*

## Plenary Session 1

- Chairpersons: *Gonzalo Calvo, Hospital Clinic I Provincial Barcelona, Spain*  
*Stefan Führung, DG Enterprise, European Commission*
- 08:15 The European Landscape for Clinical Trials  
*Diane van Vyve, EORTC, Belgium*
- 08:30 What is ICREL?  
*Ingrid Klingmann, EFGCP, ICREL Project Coordinator, Belgium*
- 09:00 Need to change the legislation? Stakeholders' views  
Non-Commercial Sponsors: *Françoise Meunier, EORTC, Belgium*  
Commercial Sponsors: *Mats Ericson, EFPIA / Wyeth Research, France*  
Ethics Committees: *Frank Wells, Cambridgeshire 4 Research Ethics Committee / EFGCP, United Kingdom*  
Competent Authorities: *Chantal Bélorgey, AFSSAPS, France*  
Patients Organisations: *Cees Smit, EGAN / VSOP, The Netherlands*
- 10:15 Coffee Break

## Plenary Session 2

- Chairpersons: *Christiane Druml, Ethics Committee of the Medical University of Vienna, Austria*  
*Stefan Führung, DG Enterprise, European Commission*
- 10:45 ICREL Results
- Methodology  
*Bruno Scherrer, Biostatistician Consultant, France*
- Impact on competent authorities  
*Gonzalo Calvo, Hospital Clinic I Provincial Barcelona, Spain*
- Impact on ethics committees  
*Johannes Pleiner, Ethics Committee of the Medical University of Vienna, Austria*
- Impact on commercial sponsors  
*Ingrid Klingmann, EFGCP, ICREL Project Coordinator, Belgium*
- Impact on non-commercial sponsors  
*Denis Lacombe, EORTC, Belgium*
- Comprehensive view of data  
*Christine Kubiak, INSERM / ECRIN, France*

12:00 Lunch

### *Break-Out Sessions*

13:00 **Impact on Commercial Sponsors**

Chair: *Willy De Greef, EuropaBio, Belgium*

Rapporteur: *Detlef Niese, Novartis, Switzerland*

**Impact on Non-Commercial Sponsors and Non-Drug Trials**

Chair: *Liselotte Hoejgaard, ESF, France*

Rapporteur: *Jacques Demotes, INSERM / ECRIN, France*

**Impact on Competent Authorities**

Chair: *Thomas Sudhop, BfArM, Germany*

Rapporteur: *Fergus Sweeney, EMEA*

**Impact on Ethics Committees and Patients' Concerns**

Chair: *Alastair Kent, GIG, United Kingdom*

Rapporteur: *Christiane Druml, Ethics Committee of the Medical University of Vienna, Austria*

14:00 Coffee Break

### *Plenary Session 3*

14:15 Reports from break-out groups & discussion

Chairpersons *Stefan Führung, DG Enterprise, European Commission*  
*Jacques Demotes, INSERM / ECRIN, France*

*Break-out Groups Rapporteurs &*  
*Ingrid Klingmann, EFGCP, ICREL Project Coordinator, Belgium*  
*Liselotte Hoejgaard, ESF, France*  
*Stefan Führung, DG Enterprise, European Commission*  
*Fergus Sweeney, EMEA*  
*Alastair Kent, GIG, United Kingdom*  
*Willy De Greef, EuropaBio, Belgium*

15:45 Closing Remarks

*Stefan Führung, DG Enterprise, European Commission*  
*Ingrid Klingmann, EFGCP, ICREL Project Coordinator, Belgium*

16:00 End of the meeting