

WP4: Riset: Legal and ethical update.

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A number of new and updated texts relevant for Riset have appeared in 2008 and the European Commission (EC) as well as the European medicines agency (EMA) are very active in this domain. The Riset consortium is regularly informed of such developments and has participated in a number of the public consultations proposed. They relate to Transplantation regulation, cell therapy regulation, immunosuppression regulation and to clinical assays in the domain of immunosuppression and cell therapy.

1. PUBLIC CONSULTATION PAPERS

- **25/01/2007: PUBLIC CONSULTATION PAPER: DRAFT OF THE COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP): “GUIDELINE ON HUMAN CELL-BASED MEDICINAL PRODUCTS”:**
 - 25/01/2007: Adoption by CHMP for release for consultation
 - 31/07/2007: Riset sent comments to the European Medicines Agency (EMA).
 - 30/05/2008: The final guideline was adopted by the CHMP¹.
 - 01/09/2008: The guideline on human cell-based medicinal products came into effect.

- **10/04/2008: PUBLIC CONSULTATION PAPER: PROPOSALS TO AMEND ANNEX I TO DIRECTIVE 2001/83/CE REGARDING ADVANCED THERAPY MEDICINAL PRODUCTS** (Implementation of the “advanced therapies” regulation, Regulation (EC) No 1394/2007²)
 - 10/04/2008: The EC published proposals opened to public consultation to adapt Part IV of Annex I to Directive 2001/83/EC³ to the specificities of advanced therapy medicinal products⁴.
 - 10/06/2008: Riset sent comments to the European Commission⁵.
 - 09/07/2008: The European Commission published the outcome of the public consultation on amendments to Annex I to Directive 2001/83/EC⁶.

- **24/04/2008: PUBLIC CONSULTATION PAPER: DRAFT OF THE COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP): “BIOMARKERS QUALIFICATION: GUIDANCE TO APPLICANTS”:**
 - 24/04/2008: The EMA published a draft of the Committee for Medicinal Products for Human Use (CHMP): “Biomarkers qualification: guidance to applicants”⁷. It was open to public consultation until June 30th, 2008. It sets up an EMA qualification process which addresses innovative drug development tools and methods and “focus on the use of Biomarkers developed by consortia, networks, public/private partnerships,

¹ <http://www.emea.europa.eu/pdfs/human/cwpw/41086906enfin.pdf>

² Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004, OJ L324, 10.12.2007, p.121.

³ Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, OJ L 311, 28.11.2001, p.67.

⁴ http://ec.europa.eu/enterprise/pharmaceuticals/advtherapies/docs/consultation-paper-nr_2008-04-08.pdf

⁵ http://ec.europa.eu/enterprise/pharmaceuticals/advtherapies/public_consultation_regulation/contributions/academic_and_public_organisations/riset.pdf

⁶ http://ec.europa.eu/enterprise/pharmaceuticals/advtherapies/pc_reg.htm

⁷ <http://www.emea.europa.eu/pdfs/human/biomarkers/7289408en.pdf>

learned societies, pharmaceutical industry for a specific intended use in pharmaceuticals R&D”⁸.

- No participation of Riset

➤ **07/05/2008: PUBLIC CONSULTATION PAPER ON THE CERTIFICATION OF QUALITY & NON-CLINICAL DATA FOR SMALL AND MEDIUM-SIZED ENTERPRISES:**

- 07/05/2008: According to Article 18 of the Regulation (EC) No 1394/2007, small and medium-sized enterprises (SMEs) developing advanced therapy medicinal products may submit to the European Medicines Agency all relevant quality and, where available, non-clinical data, for scientific evaluation and certification. The Commission, which shall lay down provisions for the evaluation and certification of such data, presented a proposal opened to public consultation in this context⁹.
- No participation of Riset
- 09/07/2008: The EC published the outcome of the public consultation on certification of quality & non-clinical data for small and medium-sized enterprises¹⁰.

➤ **04/07/2008: PUBLIC CONSULTATION PAPER ON GOOD CLINICAL PRACTICE SPECIFIC TO ADVANCED THERAPY MEDICINAL PRODUCTS:**

- 04/07/2008: Article 4 of the Regulation (EC) No 1394/2007 provides: “[...] The Commission shall, after consulting the Agency, draw up detailed guidelines on good clinical practice specific to advanced therapy medicinal products.” The EC presented proposals opened to public consultation to draft such guidance¹¹.
- 15/10/2008: Riset sent a participation of no specific comments to the European Commission¹².
- 28/10/2008: The EC published the outcome of the public consultation on good clinical practice specific to advanced therapy medicinal products¹³.

➤ **22/07/2008: PUBLIC CONSULTATION PAPER ON THE REVISED CLINICAL TRIAL APPLICATION FORM REGARDING ADVANCED THERAPY INVESTIGATIONAL MEDICINAL PRODUCTS:**

- 22/07/2008: The standard template for the clinical trial application form defined in Annex 1 to the “Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial¹⁴” need to be adapted to incorporate the changes entailed by Regulation (EC) No 1394/2007. The EC published a draft proposal for such amendments¹⁵.
- 15/10/2008: Riset sent a participation of no comments to the EC¹⁶.
- 22/10/2008: The EC published the outcome of the public consultation on the revised clinical trial application form as regards advanced therapy investigational medicinal products¹⁷.

⁸ Scope of the “Biomarkers qualification: guidance to applicants”.

⁹ http://ec.europa.eu/enterprise/pharmaceuticals/advtherapies/docs/2008_05_cp/consultationpaper-nr-2008-05-05.pdf

¹⁰ http://ec.europa.eu/enterprise/pharmaceuticals/advtherapies/pc_certif.htm

¹¹ http://ec.europa.eu/enterprise/pharmaceuticals/advtherapies/docs/2008_07/Consultation%20paper-NR-2008-07-02.pdf

¹² http://ec.europa.eu/enterprise/pharmaceuticals/clinicaltrials/docs/pcr_28-10-2008/riset.pdf

¹³ http://ec.europa.eu/enterprise/pharmaceuticals/clinicaltrials/clinicaltrials_key.htm

¹⁴ http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/11_ca_14-2005.pdf

¹⁵ http://ec.europa.eu/enterprise/pharmaceuticals/advtherapies/docs/consultation_paper-2008-07-22.pdf

¹⁶ http://ec.europa.eu/enterprise/pharmaceuticals/clinicaltrials/docs/pcr_22-10-08/riset.pdf

➤ **03/07/2008: PUBLIC CONSULTATION PAPER ON THE DATA FIELDS CONTAINED IN THE “EUDRA CT” CLINICAL TRIALS DATABASE TO BE INCLUDED IN THE “EUDRAPHARM” DATABASE ON MEDICINAL PRODUCTS AND MADE PUBLIC:**

- 03/07/08: The EC published a draft list of fields contained in the “EudraCT” clinical trials database to be included in the “EudraPharm” database on medicinal products and made public¹⁸, in accordance with Article 57 (2) of Regulation (EC) No 726/2004¹⁹.
- 15/10/2008: Riset sent a participation of no comments to the EC²⁰.
- 21/10/2008: The EC published the outcome of the public consultation on the data fields contained in the 'EudraCT' clinical trials database to be included in the 'EudraPharm' database on medicinal products and made public²¹.

2. EUROPEAN UNION (EU) LEGISLATION

➤ **08/12/2008: EU LEGISLATION: PROPOSAL OF A DIRECTIVE ON STANDARDS OF QUALITY AND SAFETY OF HUMAN ORGANS INTENDED FOR TRANSPLANTATION:**

- 08/12/2008: The EC adopted a proposal of a Directive on standards of quality and safety of human organs intended for transplantation²² and an Action plan on Organ Donation and Transplantation²³. Three challenges are addressed: improving the quality and safety of organs across Europe, increasing organ availability and making transplant systems more efficient and accessible.

I- EU GUIDELINES:

➤ **30/05/2008: ADOPTION OF THE FINAL GUIDELINE ON HUMAN CELL-BASED MEDICINAL PRODUCTS²⁴:**

- 01/09/2008: It came into effect.

➤ **05/11/2008: PUBLICATION OF ADDITIONAL GUIDELINES ON GOOD CLINICAL PRACTICES (GCP) INSPECTIONS:**

- 05/11/2008: Article 29 of the Directive 2005/28/EC provides the EC shall publish guidance on the conduct of inspections by the competent authorities of the different Member States. The EC has published Annex V (Phase I units)²⁵ and VII (Bioanalytical part, Pharmacokinetic and Statistical Analyses of Bioequivalence

¹⁷ http://ec.europa.eu/enterprise/pharmaceuticals/clinicaltrials/clinicaltrials_key.htm

¹⁸ http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/docs/doc2008/2008_07/consultation_draft_field-2008-07-16.pdf

¹⁹ Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, OJ L 136, 30.04.2004, p.1.

²⁰ http://ec.europa.eu/enterprise/pharmaceuticals/clinicaltrials/docs/clintrials_resp/riset_21-10-2008.pdf

²¹ http://ec.europa.eu/enterprise/pharmaceuticals/clinicaltrials/clinicaltrials_key.htm

²² Proposal for a Directive of the European Parliament and of the Council on standards of quality and safety of human organs intended for transplantation, 08/12/08, COM (2008)818 final: http://ec.europa.eu/health/ph_threats/human_substance/oc_organs/docs/organs_directive_en.pdf

²³ Communication from the Commission, Action plan on Organ Donation and Transplantation (2009-2015) : Strengthened Cooperation between Member States, 08/12/08, COM (2008)819 final: http://ec.europa.eu/health/ph_threats/human_substance/oc_organs/docs/organs_action_en.pdf

²⁴ <http://www.emea.europa.eu/pdfs/human/cwpw/41086906enfin.pdf>

²⁵ http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/2008_11/vp110_an5_10-2008.pdf

Trials)²⁶ to these guidelines in Eudralex- Volume 10²⁷; and it has issued Guidelines for the procedure for standardisation of GCP inspection entries in EudraCT²⁸.

➤ **16/12/2008: PUBLICATION OF GUIDANCE DOCUMENTS APPLYING TO CLINICAL TRIALS:**

- 16/12/2008: Revision and publication of the “Questions & Answers” Document in the EudraLex chapter on clinical trials²⁹.

II- CONFERENCE AND WORKSHOPS:

➤ **29-30/09/2008: “INNOVATION FORUM” organised by the Drug Information Association (DIA) in London:**

- 29-30/09/2008: The objectives of the conference were to “provide an update on the initiatives in Europe to support innovation in research and development, share the FDA experience with the implementation of the Critical Path Initiative and coordination with the EU initiatives, provide a platform to discuss the implementation of the European Parliament and Council Regulation on Advanced Therapy and the EMEA draft technical guidelines”³⁰.

➤ **03/02/2009: 1st EMEA WORKSHOP ON ADVANCED THERAPY MEDICINAL PRODUCTS IN LONDON**³¹:

- 03/04/2009: This workshop will present “an overview of the new EU legislation on ATMPs and its implementation, dossier requirements for ATMPs and the evaluation procedure for marketing authorisation. There will also be a session on how to obtain classification as an ATMP and request EMEA certification of quality and non-clinical data”³².

²⁶ http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/2008_11/vol10_an7_10-2008.pdf

²⁷ http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol10_en.htm

²⁸ http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/2008_11/2008_09_16_guideline_procedure-cgp-eudract.pdf

²⁹ http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/q%26a_v2.pdf

³⁰ <http://www.diahome.org/DIAHOME/Education/FindEducationalOffering.aspx?productID=16917&eventType=Meeting&rpex=N&kw=innovation%20forum&st=09-29-2008#>

³¹ Agenda: <http://www.emea.europa.eu/pdfs/conference/flyers/sme3/61666908en.pdf>

³² <http://www.emea.europa.eu/htms/human/mes/advancedtherapies.htm>