SUBMISSION OF COMMENTS ON 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 TRIAL

COMMENTS FROM The EU FP6 integrated project "RISET" : Reprogramming the immune system for the establishment of tolerance, Contract N° 512090 IP, web site : www.risetfp6.org . Coordinator: Pr. Michel Goldman/Kathryn Wood.

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Document prepared with the help of Aurélie Mahalatchimy (PhD in Law).

The document was highlighted by Kathryn Wood to the RISET consortium involved in clinical trials using cell therapy and in regulatory and ethical issues, upon suggestion by Anne Cambon-Thomsen. It was posted on the website and the following comments have been made.

GENERAL COMMENTS

Context: One WP in RISET (WP3), under the leadership of Lucienne Chatenoud is dedicated to clinical trials related to 1) tolerance induction. 2) Minimisation of immunosuppression. 3) Refining the use of tolerogenic drugs. Ten clinical trials are underway or have been performed (3 cell-therapy based; 7 others ; for details see : http://www.risetfp6.org/cgi-bin/WebObjects/Awo3.woa/2/wo/1jhtdl1dgIRHfxZNTmsSEM/4.0.27.5.2.12.1.7.0.0.0.0.0.0.0.0.1.10.16.1.0.1.4.0.0.1)

People involved in this WP were asked to comment on the public consultation paper, but this possibility was also given to all partners.

Some comments of general relevance are as follows:

RISET welcomes the opportunity to review this draft on 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 trial. We appreciate the clarification provided by this draft and consider it very useful particularly regarding the meaning of the words "amendments" and "substantial" and the examples given. It clarifies several previously ambiguous notions.

We also have some specific comments.

SPECIFIC COMMENTS ON TEXT		
PROPOSALS TO AMEND ANNEX I TO DIRECTIVE 2001/83/CE AS REGARDS ADVANCED THERAPY MEDICINAL PRODUCTS		
paragraph no.	**Comment and Rationale**	**Proposed change (if applicable)** **Proposed changes appear in CAPITAL LETTERS**
1.2. p. 6 § 1	"Directive 2001/20/EC also applies to medicinal products for paediatric population." A reference to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use mentioned page 10 should be added	
1.2. p. 6 § 1	"To draw the "borderline" between these sectoral legislations, the established criteria as set out in the jurisprudence of the European Court of Justice and the applicable guidelines apply." A list of applicable guidelines should be provided.	
2.6. p. 14 § 1	"For an international trial where the medicinal product to be used in each Member State is the one authorised at a national level and the SmPC varies among Member States, the sponsor should chose one SmPC to replace the IB for the whole clinical trial." Is there any guidance on the criteria of choice of this SmPC? (particularly with reference to 2.8.3. of the draft)	
4.3. p. 31	"However, the clinical trial summary report can be submitted subsequently to the end of trials notification." A deadline should be indicated to submit the clinical trial summary report in case it is not transmitted at the time of the	

	end of trials notification.	
4.4 p.31	“If a new event occurs after the termination of the trial that is likely to change the risk/benefit analysis of the trial and could still have an impact on the trial participants, the sponsor should notify the national competent authority and Ethics Committee of the Member State concerned and provide a proposed course of action.” When the trial is completed in several participating centres, all competent authorities of Member States involved in the clinical trial should be notified.	