MINISTERIO
DE SANIDAD, POLÍTICA SOCIAL
E IGUALDAD

agencia española de
medicamentos y
productos sanitarios

CAT Stakeholders workshop

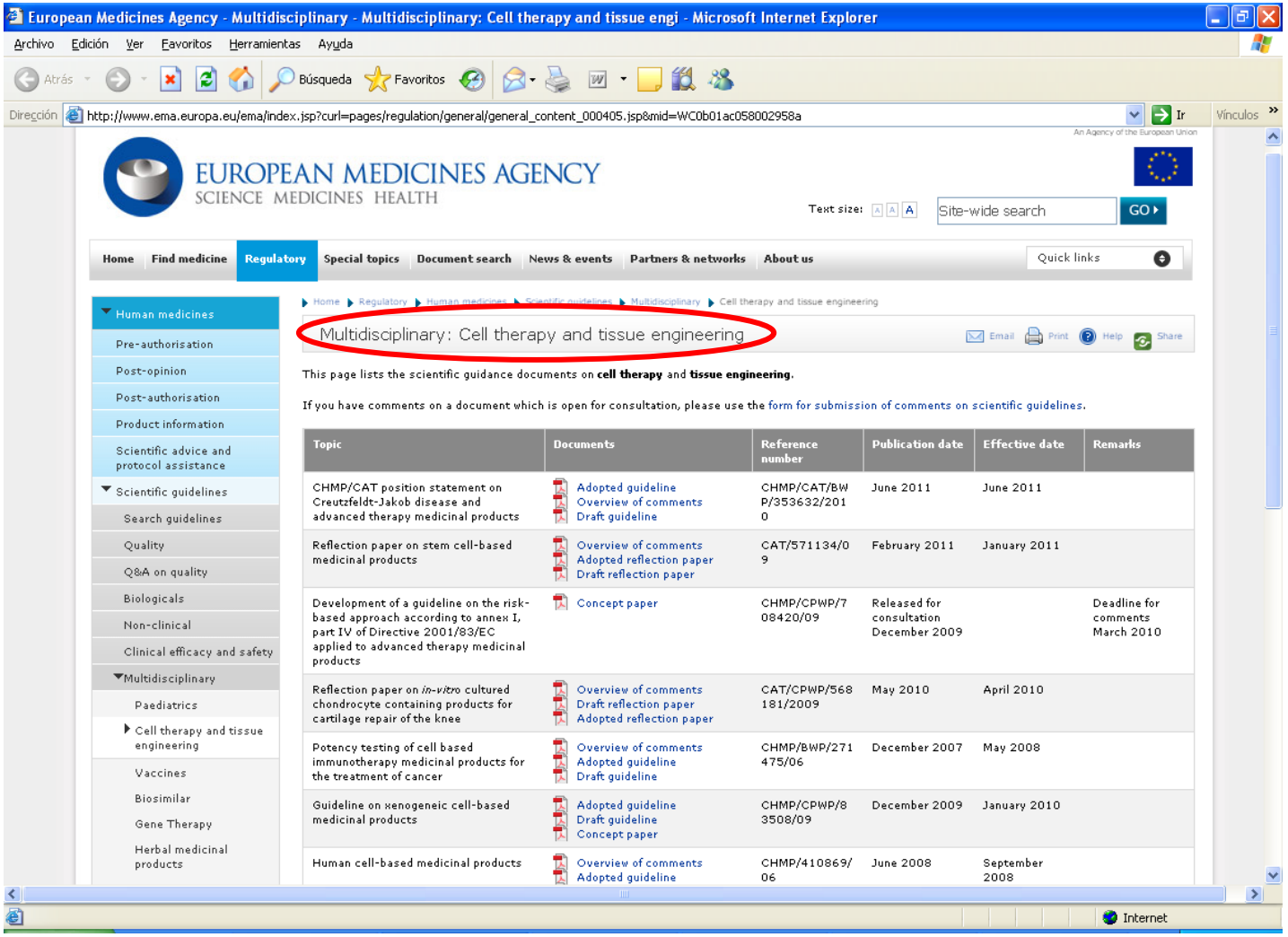
Focus Groups: a model for a fruitful interaction between CAT and its stakeholders

Interactive flow-chart for Gene Therapy guidelines

Pablo de Felipe

London, 12 January 2012

Adv. Ther. guidelines at the EMA webpage



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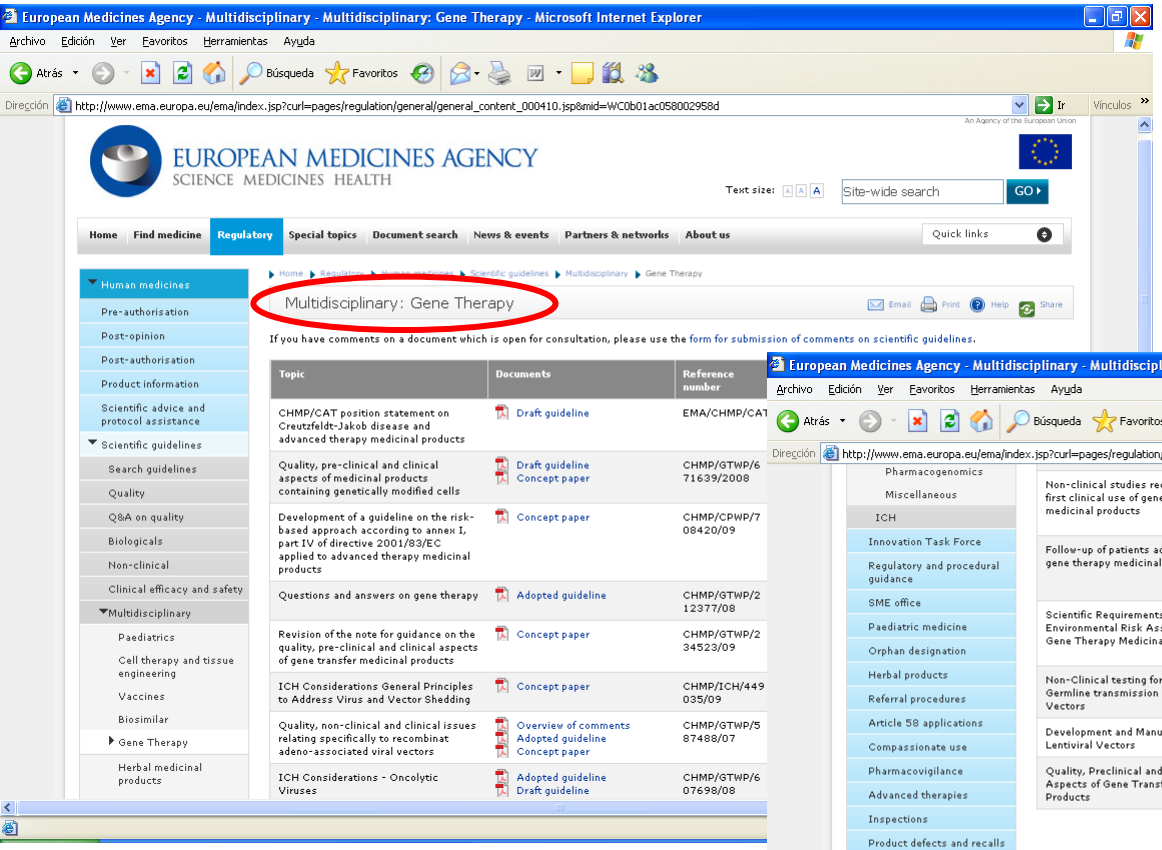
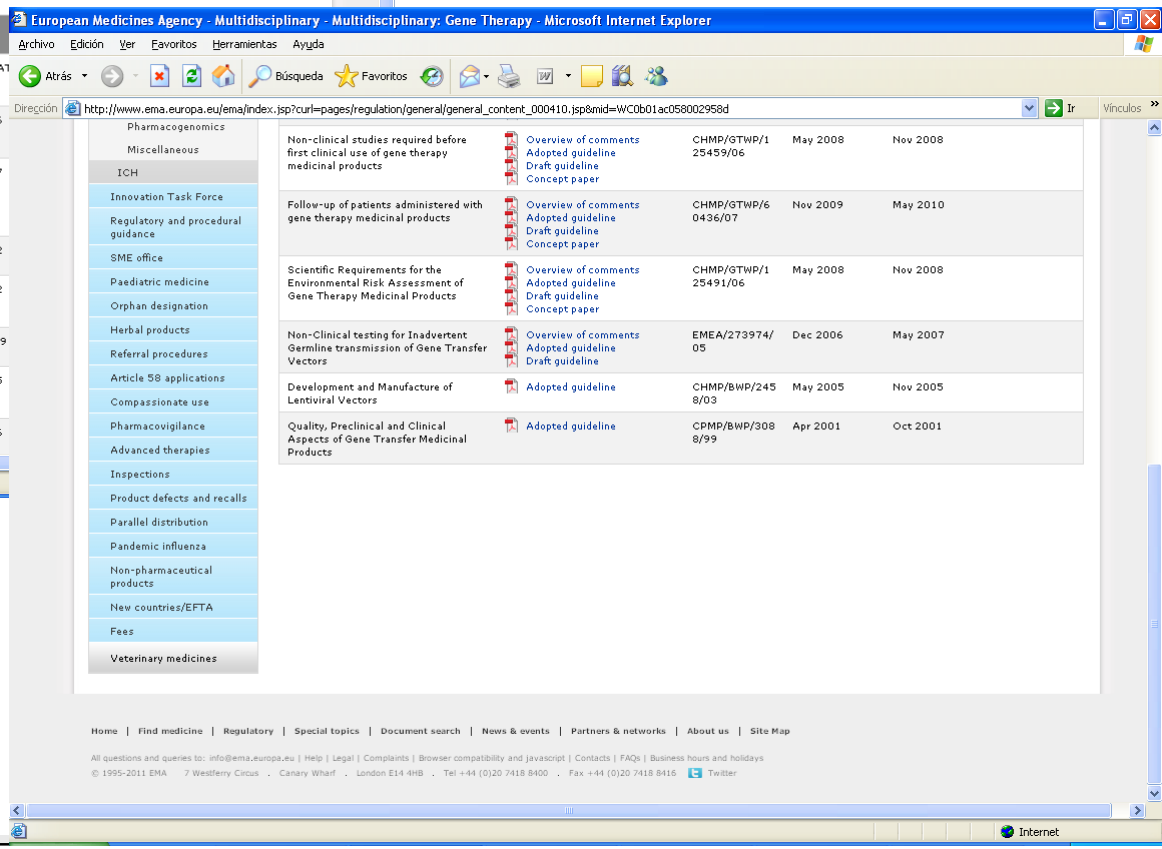




Flow-chart 1st step: list and classification

General

-"Note for guidance on the quality, preclinical and clinical aspects of gene transfer medicinal products" **(CPMP/BWP/3088/99) Q NC C**

- "Questions and answers on gene therapy" **(CHMP/GTWP/212377/08) Q NC**

Certification (only for Q or for Q+NC)

- "Procedural advice on the certification of quality and non-clinical data for small and medium sized enterprises developing advanced therapy medicinal products" **(EMA/CAT/418458/2008/corr.) Q NC**

- "Guideline on the minimum quality and non-clinical data for certification of advanced therapy medicinal products" **(EMA/CAT/486831/2008/corr.) Q NC**

First in human

- "Guideline on the non-clinical studies required before first clinical use of gene therapy medicinal products" **(EMEA/CHMP/GTWP/125459/2006) NC**

Flow-chart 1st step: list and classification

Marketing authorisation application (MAA) (1/2)

Vectors

- "Guideline on development and manufacture of lentiviral vectors" **(CHMP/BWP/2458/03) Q**
- "ICH considerations: oncolytic viruses" **(CHMP/ICH/607698/08) Q NC C**
- "Reflection paper on quality, non-clinical and clinical issues related to the development of recombinant adeno-associated viral vectors" **(CHMP/GTWP/587488/07) Q NC C**
- General chapter of the Eur. Ph.: "Gene transfer medicinal products for human use" **(01/2010:51400) Q**

Gene therapy products with modified somatic cells

- "Guideline on quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells" **(CHMP/GTWP/671639/2008) Q NC C** Draft

Risk of germline transmission

-"Guideline on non-clinical testing for inadvertent germline transmission of the gene transfer vectors" **(EMEA/273974/2005) NC**
- "ICH Considerations: General principles to address the risk of inadvertent germline integration of gene therapy vectors" **(CHMP/ICH/469991/2006) NC**

Flow-chart 1st step: list and classification

Marketing authorisation application (MAA) (2/2)

Post-administration

- "Guideline on follow-up of patients administered with gene therapy medicinal products" **(EMEA/CHMP/GTWP/60436/2007) C**
-"Guideline on safety and efficacy follow-up - risk management of advanced therapy medicinal products" **(Doc. Ref. EMEA/149995/2008) C**
- "ICH Considerations: General principles to address virus and vector shedding" **(CHMP/ICH/449035/09) C**

Environmental risk

- Guideline on scientific requirements for the environmental risk assessment of gene therapy medicinal products" **(EMEA/CHMP/GTWP/125491/2006)**
- "Guideline on environmental risk assessments for medicinal products consisting of, or containing, genetically modified organisms (GMOs)" **(EMEA/CHMP/BWP/473191/2006-corr)**

Flow-chart 1st step: list and classification

Other relevant guidelines (1/3)

Cell therapy guidelines

-Guideline on human cell-based medicinal products **(EMEA/CHMP/410869/2006)**
- Guideline on xenogeneic cell-based medicinal products **(EMEA/CHMP/CPWP/83508/2009)**
- Reflection paper on stem cell-based medicinal products **(EMA/CAT/571134/2009)**

Reagents/Materials

-ICH Q5B: note for guidance on quality of biotechnological products: analysis of the expression construct in cell lines used for production of r-DNA derived protein products **(CPMP/ICH/139/95)**
-Note for Guidance on the Use of Bovine Serum in the Manufacture of Human Biological Medicinal Products **(CPMP/BWP/1793/02)**
- ICH Q5D: Quality of Biotechnological Products: Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products **(CPMP/ICH/294/95)**
-Position Statement on the Use of Tumourigenic Cells of Human Origin for the Production of Biological and Biotechnological Medicinal Products **(CPMP/BWP/1143/00)**
- Use of Transgenic Animals in the Manufacture of Biological Medicinal Products for Human use **(3AB7A)**

Development

- Development pharmaceutics for biotechnological and biological products **(CPMP/BWP/328/99)**. Annex to Note for guidance on development pharmaceutics **(CPMP/QWP/155/96)**

Flow-chart 1st step: list and classification

Other relevant guidelines (2/3)

Viral safety related guidelines (for biological and biotechnological products)

-Note for guidance on virus validation studies: the design, contribution and interpretation of studies validating the inactivation and removal of viruses (**CPMP/BWP/268/95** or **3AB8A**)

- ICH Topic Q5A: Note for guidance on quality of biotechnological products: viral safety evaluation of biotechnology products derived from cell lines of human or animal origin **(CPMP/ICH/295/95)**

- "Guideline on quality, non-clinical and clinical aspects of live recombinant viral vectored vaccines" **(EMA/CHMP/VWP/141697/2009)**

TSE/CJD safety related guidelines

-Note for guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products **(EMEA/410/01 Rev. 3) (Official Journal of the European Union - 2011/C 73/01)**

- CHMP/CAT position statement on Creutzfeldt-Jakob disease and advanced therapy medicinal products **(EMA/CHMP/CAT/BWP/353632/2010)** Draft

Changes in the manufacturing process

-ICH Topic Q5E: Note for guidance on biotechnological/biological products subject to changes in their manufacturing process **(CPMP/ICH/5721/03)**

- Reflection paper on changes during development of gene therapy medicinal product **()** Draft

Flow-chart 1st step: list and classification

Other relevant guidelines (3/3)

Testing

- Tests on samples of biological origin **(3AB11A)**
- ICH Q6B: Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products **(CPMP/ICH/365/96)**
- Guideline on potency testing of cell based immunotherapy medicinal products for the treatment of cancer **(EMEA/CHMP/BWP/271475/2006)**
- ICH 5QC: Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products **(3AB5A or CPMP/ICH/138/95)**

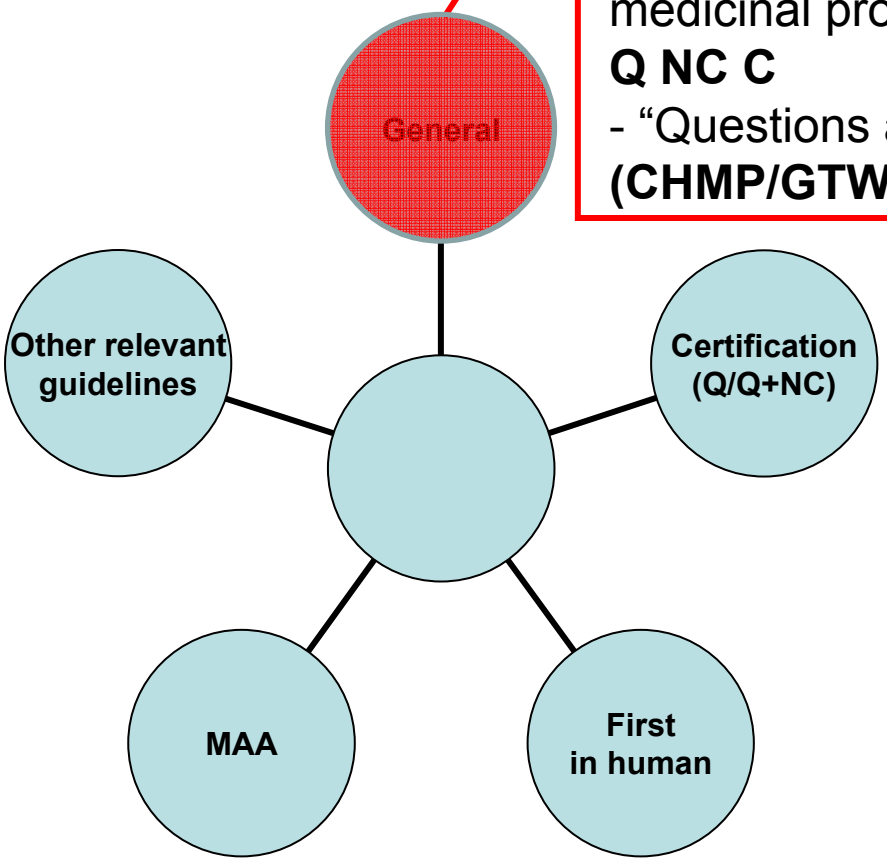
Flow-chart 1st step: list and classification

NOTE:

This flowchart only includes the currently applicable guidelines. It is acknowledged that in the EMA website all historical guidelines can be found.

The guidelines included in this flow chart are those specific for gene therapy medicinal products and those related with biotechnological and biological products where similar principles can be applied to GTMPs. Other general ICH and EMA guidelines, in particular for non clinical, clinical aspects, paediatrics and orphans as well as European Pharmacopeia monographs and chapters might be applicable.

Flow-chart 2nd step: proposal of arrangement



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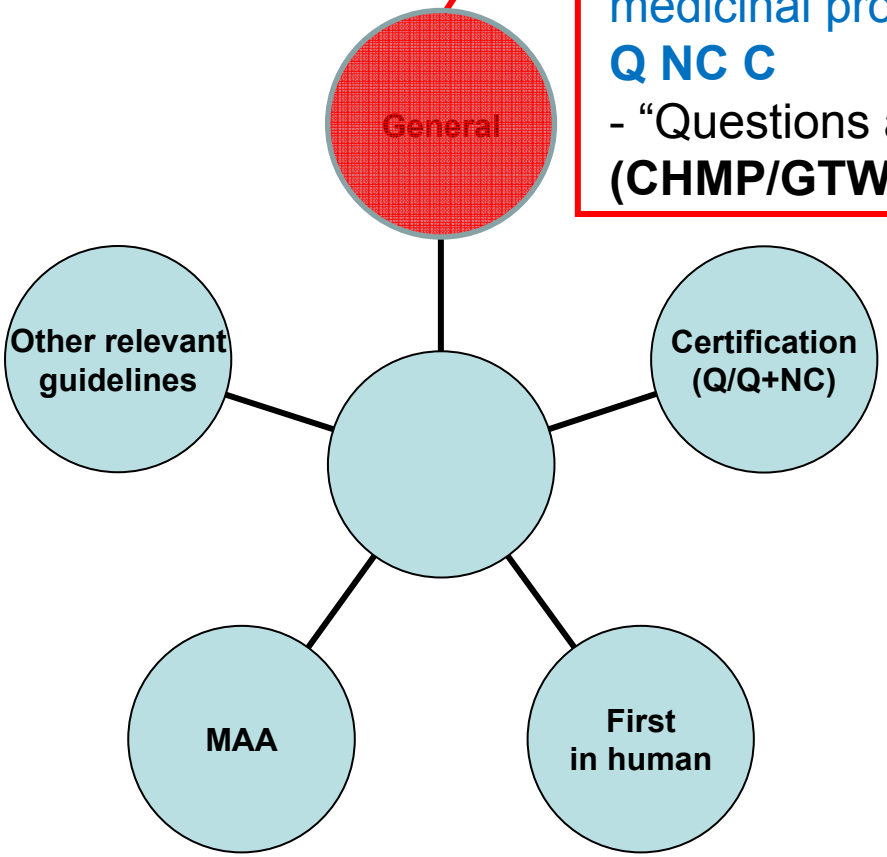

General

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Q NC C

- "Questions an

(CHMP/GTWP/

The European Agency for the Evaluation of Medicinal Products
Evaluation of Medicines for Human Use

London, 24 April 2001
CPMP/BWP/3088/99

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS (CPMP)

NOTE FOR GUIDANCE ON THE QUALITY, PRECLINICAL AND CLINICAL ASPECTS OF GENE TRANSFER MEDICINAL PRODUCTS

DISCUSSION IN THE BIOTECHNOLOGY WORKING PARTY (BWP)	June – December 1999
DISCUSSION IN THE SAFETY WORKING PARTY (SWP)	June 1999
DISCUSSION IN THE EFFICACY WORKING PARTY	July – November 1999
TRANSMISSION TO CPMP	December 1999
RELEASE FOR CONSULTATION	December 1999
DEADLINE FOR COMMENTS	June 2000
DISCUSSION IN THE EFFICACY WORKING PARTY (EWP)	September 2000
DISCUSSION IN THE SAFETY WORKING PARTY (SWP)	February 2001
DISCUSSION IN THE BIOTECHNOLOGY WORKING PARTY (BWP)	March 2001
WRITTEN PROCEDURE WITH SAFETY WORKING PARTY (SWP)	April 2001
TRANSMISSION TO CPMP	April 2001

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¡THANK YOU!

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London, 12 January 2012