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**Meeting of Competent Authorities
On Tissues and Cells
19-20 October 2009**

Summary report

The fourth meeting of Competent Authorities on Tissues and Cells was convened on 19 and 20 October 2009 under the Chairmanship of Patricia BRUNKO.

All Member States except Luxembourg and Slovenia were represented at the meeting; were also represented: Iceland, Liechtenstein, Norway, Turkey and Croatia as well the Council of Europe.

1. ADOPTION OF THE AGENDA

The Chairperson highlighted that the aim of the meeting was to discuss the progress and challenges encountered in the transposition and implementation of the Tissues and Cells Directives in the Member States, to have a discussion on a number of proposals by the Commission related to the implementation of these Directives and to share information on programmes and initiatives related to this area.

The agenda was adopted without change.

2. TRANSPOSITION AND IMPLEMENTATION OF THE TISSUES AND CELLS DIRECTIVE

2.1. Update on transposition and infringement procedures.

The Commission presented the latest data regarding transposition of the Tissues and Cells Directives. 26 Member States have completely transposed Directive 2004/23/EC, 25 Member States have completely transposed Directives 2006/17/EC and 2006/86/EC. There are currently 5 infringement procedures open for partial and non transposition of the Directives in two Member States.

2.2. Update on report templates that will be sent to Member States

The Commission informed the Member States on next *Report templates*¹ that will be sent to them for completion in the coming months:

- A report template on "Voluntary unpaid donation", in accordance with Member States' reporting obligation provided for in Article 12(1) of Directive 2004/23/EC will be sent at the end of November/beginning of December.
- In order to adequately monitor the transposition of the Tissues and Cells Directives, a "Report template: Transposition concordance table" will be sent at the end of November/beginning of December.

2.3. Update on procedure for the adoption of Report on Implementation of Tissues and Cells Directives

The Commission informed the Member States on the procedure for the adoption of the first report on implementation of the Tissues and Cells Directive (based on the information submitted by the Member States) and invited the Member States to provide comments on the report by 26 October.

3. INSPECTIONS

3.1. State of play of Inspection guidelines

During the previous meeting of Competent Authorities, the Member States agreed that the inspection measures could be developed through two different documents: a Commission Decision on guidelines for inspections covering the core elements decided by Comitology and a detailed Operational Manual agreed by consensus of the Competent Authorities.

The Commission presented the developments in the inspection measures since last meeting of Competent Authorities in May:

After a thorough revision by the Working Group (WG) on Inspection guidelines, the Operational Manual was sent to stakeholders and Competent Authorities for consultation in August 2009. The final drafts were sent to the Member States prior to this meeting of Competent Authorities.

The texts were presented to the Member States.

Operational Manual on inspections:

All Member States agreed on the Operational Manual. Germany still needed to consult the regional inspectorates before confirming official agreement by the 10th of November. The Operational Manual will be sent for translation and afterwards will be published on the SANCO website.

The Operational Manual should be used by inspectors and could be eventually modified in accordance with experience.

¹ Questionnaire developed by the Commission based on legal provisions or necessary to monitor the implementation and transposition process (See point 3 of minutes of CA meeting 27-28 May 2009).

Decision on guidelines for inspections

Member States also supported the content of the Decision and strongly supported the division among the Decision and the Operational Manual. The Decision will follow the normal procedure for its adoption by Comitology procedure.

3.2. Inspections of Storage tissue establishments

During the last meeting of Competent Authorities, France asked for clarification on the need to accreditate/designate/authorise/license and therefore inspect storage for end-use repositories (in hospital or other health care establishments).

Some Member States highlighted the fact that if all these repositories need to be inspected, resources to inspect higher risk activities will have to be deviated to perform inspections to the repositories.

On the other hand, appropriate storage conditions, traceability and recall systems should be ensured in all cases.

Currently, different approaches are followed by Member States:

- Some Member States do not accreditate/designate/authorise/license these repositories; the responsibilities are within the health care establishment.
- Some Member States ask for the repositories to be accredited/designated/authorised/licensed if the product is going to be stored for more than 48 hours; or the product has special storage conditions.
- Some Member States give to the Tissue Establishment the responsibility to control that the products are adequately stored in the health care establishment.

By analogy, it was mentioned that the Blood Directive² establishes the "hospital blood banks" to address this issue. According to Article 6 of this Directive, a hospital blood bank needs to comply with the same requirements as a blood establishment in terms of "Personnel", "Quality systems", "Documentation", "Traceability", "Notification of serious adverse events and reactions", "Storage, transport and distribution" and "Data protection".

The Commission also explained that distribution is considered a step undertaken by a tissue establishment towards sites of utilisation and medical application (e.g. hospitals, dentists), potentially passing through a repository/storage room. Further distribution out of these repositories is not allowed, as this is to be undertaken by the tissue establishment. In order to ensure traceability, tissue establishments are to register destinations of medical application, and those destinations are to register the patients that received the substances.

The Commission is currently preparing an explanatory note on the terms "transport", "storage" and "distribution".

² Directive 2002/98/EC setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC.

4. EUROPEAN GOOD TISSUE PRACTICES PROJECT (GTPs)

The aim of the project is to develop detailed common "Good tissue practices" for European tissue establishments (Ocular, Cardiovascular, Musculoskeletal, Skin) as well as a training module for personnel of tissue establishments.

Science and retrieval techniques evolve very rapidly and tissues and cells are increasingly exchanged between Member States and third countries. The purpose of the GTPs project is not to give very detailed guidance that would be quickly outdated, but to provide some core aspects that might help inspectors and professionals to identify good tissue practices in the preparation process of tissues and cells. The project will address specific issues like validation of preparation procedures and air quality conditions.

Member States recognised the difficulties of having updated guidance on procurement and processing procedures. However, they welcomed the content of the project and appreciated having guidance on how to assess the specific preparation processes.

For some Member States, the project should only focus on quality and safety (being this the scope of the Directive), leaving efficacy aside. However, for other Member States efficacy is inherent to validation, in particular when this is based on retrospective evaluation of the clinical results for tissues supplied by the tissue establishment.

The project leader was invited to present and discuss the preliminary results of the project to the Competent Authorities within one year.

For more information, please go to: <http://eurogtps.com/>.

5. PROPOSAL FOR A QUALITY SYSTEM MANUAL FOR BLOOD AND TISSUES & CELLS

The Commission informed the Member States on a proposal for a Manual on quality systems for blood and tissues & cells establishments.

Member States did not welcome a common approach for blood and tissues/cells. As Directive 2006/86/EC has developed the minimum requirements for tissue establishment's quality systems, it was concluded not to move forward with any further guidance on quality systems for tissues and cells.

6. UPDATE ON EURO CET

Italy made an update on the current activities performed by EURO CET (European Registry for Competent Authorities for Tissues and Cells) and on the data collected. Competent Authorities notify the tissue establishments in their territory to EURO CET. EURO CET has recently reached an agreement with EBMT³ and ESHRE⁴ in order to have their tissues establishments added to the database.

³ European Group for Blood and Marrow Transplantation.

⁴ European Society of Human Reproduction and Embryology.

It is expected that each Competent Authority ensures that tissue establishments reported to EURO CET have been authorised and comply with EU legislation. The idea of having an Authorisation Certificate (as provided in Annex 10 of the Operational manual on inspections) for any tissue establishments on the EURO CET database was discussed.

The EURO CET manager invited other participants to volunteer and help the Italian Competent Authority in managing and governing the EURO CET database.

To prepare for reflections on further steps; the Commission will further analyse the different legal provisions in relation to a European registry.

For more information, please go to: <http://www.eurocet.org/>.

7. VIGILANCE

7.1. Presentation of a Rapid Alert system

During the last meeting of Competent Authorities, Denmark presented a draft procedure for a rapid alert system. The draft procedure was sent for consultation to all Competent Authorities during summer time. A version compiling suggestions and comments was sent to the Competent Authorities prior to this meeting.

Denmark presented the resulting document and several practical issues were discussed. A pilot phase will be launched at the beginning of next year.

7.2. Information on CIRCA systems

The Commission informed the Member States about the creation of two CIRCA systems:

- CIRCA-CAsTC: will allow sharing all documents prior to meeting of Competent Authorities. Any other relevant information could also be included.

Current representatives of the Competent Authorities will be provided with the general instructions for the creation of this CIRCA-CAsTC.

- CIRCA-RATC: will allow managing the rapid alerts.

Member States will be asked to assign the official contacts for rapid alerts and to provide a functional mail address and a phone number for each contact point.

7.3. Serious adverse reactions and events: Annual report 2008

The Commission informed that around 20 Member States had submitted the 2008 "REPORT TEMPLATE on Serious Adverse Events and Reactions for Tissues and Cells". Based on the information submitted, the Commission will make a summary report that will be provided to the Competent Authorities in accordance with Article 7 of Directive 2006/86/EC.

7.4. Update on the development of the European Coding System

The Commission gave an update on the development of the European coding system. In order to perform the impact assessment, RAND, an external consultant, was asked to

collect data and facts on different elements of a European coding system. Several regulators and operators will be contacted and interviewed by RAND in November.

The Commission will convene a meeting of the Coding working group in the first half of 2010.

8. REPORTING OBLIGATIONS (ART. 10(1))

During the last meeting of Competent Authorities, the Danish delegation asked whether the requirement of having tissue establishments' annual reports publicly available as requested by Article 10(1) of Directive 2004/23/EC could be fulfilled with the publication of a report summarising the individual reports received by the Competent Authority.

In this context, some Member States mentioned their reluctance to publish or make available individual tissue establishments annual reports as they might disclose sensitive commercial information.

The Commission informed the Member States that it is possible to publish only summary reports provided that they inform the public that individual reports can be made available and that Member States have an up-to-date registry of accredited/designated/authorised/licensed tissues and cells.

9. UPDATE ON ADVANCED THERAPIES MEDICINAL PRODUCT REGULATION

The Commission updated the delegations on the implementation of the Regulation on Advanced Therapies Medicinal Products (Regulation (EC) No 1394/2007).

The Competent Authorities stressed the need to ensure that any implementing measure of this Regulation should comply with the provisions of the Tissues and Cells Directives regarding donation, procurement and testing at any stage of development of advanced therapies medicinal products.

It was proposed to establish a more integrated and complementary approach between regulators in the fields of tissues and cells and advanced therapies.

10. OTHER BUSINESS

10.1. Testing of partner donation (not for direct use): "is it necessary to repeat the testing at the time of each donation?" (AT)

The Commission explained to the Member States that annex III of Directive 2006/17/EC requires to perform the testing of the donor at the time of each donation of gametes in order to assess the risk of cross contamination during cryo-preservation.

Some Member States argued that this is costly and not needed. A regular mandatory fixed testing (e.g. every 2 years, every 6 months) was said to be sufficient to control cross contamination.

The Commission asked the Member States to provide scientific evidence that proves that testing at the time of each donation is not offering additional safety and is costly.

10.2. "What is considered to be the starting point for embryonic stem cell lines: the donors of the gametes or the embryonic stem cell lines?" (UK)

Frozen embryos that are not usable for Assisted Reproductive Technologies (ART), might be used in some Member States for the development of embryonic stem cell lines which end up in clinical trials or advanced therapies.

These tissues and cells are subject to the Tissues and cells Directives as far as donation, procurement and testing is concerned; to the Directive 2001/20/EC where used for Clinical Trials and to Regulation 1394/2007 when used as Advanced Therapies Medicinal Products. As these regulations fall under different authorities or bodies (Commission, National Competent Authorities and EMEA), the need for a multi-party discussion was expressed in order to ensure complementarities.

An important point to align on between authorities and bodies relates to the stage at which to test. United Kingdom stated that they consider that the starting point for the embryonic stem cell lines are the donors and perform the testing in accordance with Directive 2006/17/EC.

The Commission referred to the discussion under point 10.1 and reaffirmed that as embryos used for stem cell lines have been frozen, there is a legal requirement to test the donors at moment of donation according to Annex III of Directive 2006/17/EC.

10.3. Question about paid donors (RO)

The Romanian Ministry had informed the Commission on a case regarding suspicion of collection of female eggs (ovocytes) from paid donors and wanted to know whether other Member States have experience on similar cases.

The Commission invited the Member States to provide information on the issue by 31 November to the Romanian Competent Authority.

10.4. Question about frozen embryos (HR)

The Croatian representative asked the Commission about which EU Member States do not allow freezing embryos.

Greece, Germany and Lithuania do not allow freezing of embryos. Italy allows freezing under certain conditions.

10.5. Facial transplant: Tissue or organ

The question whether composite and facial transplant should be considered organs or tissues was discussed.

For most Member States, facial transplants should be considered as composite tissue transplants, multi-tissues or tissues with special status. Composite tissue transplants require processing similar to organs; however composite tissue transplants are not defined as organs as they fulfil no physiological life-saving function.

It was highlighted that independently of the classification, patient safety should always be the driver of any possible consideration. No conclusion was reached at the meeting.

10.6. **Authorised representatives for commercial human bone substitutes (DK)**

Denmark presented a proposal for an amendment to Directive 2004/23/EC in order to manage the distribution of commercial bone substitutes.

These products are put on the EU market through one distributor within one Member State. The Commission explained that Directive 2004/23/EC clearly stipulates that the import/export, storage and distribution activities can only be performed by tissue establishments. All distributors of commercial bone substitutes in all EU Member States therefore need to comply with the EU legislation and need to be accredited/designated/authorised/licensed by the National Competent Authorities accordingly.

10.7. **EATB announcement (PL)**

Poland, representing the EATB, explained the future creation of training programmes and European Certification for tissue bankers.

10.8. **EUSTITE final Conference (IT)**

Italy announced the final conference of the EUSTITE project that will take place in Warsaw on 1st to 4th December and invited all Competent Authorities to attend.

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The next Competent Authorities meeting was provisionally set for 8-9 March 2010.


Patricia BRUNKO