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Meeting of Competent Authorities On Tissues and Cells

27-28 May 2009

Summary report

The third meeting of Competent Authorities on Tissues and Cells was convened on 27 and 28 May 2009 under the Chairmanship of Patricia BRUNKO.

All Member States except Luxembourg, Bulgaria and Cyprus were represented at the meeting; were also represented: Liechtenstein, Norway, Turkey, Croatia and the Council of Europe.

1. ADOPTION OF THE AGENDA

The Chairperson welcomed the delegations. 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. UPDATE OF THE COMPETENT AUTHORITY OF EACH MEMBER STATE

Each delegation presented a brief overview of its structures, related responsibilities and underlined the main developments since the last Competent Authorities meeting.

3. GENERAL DISCUSSION ON THE TRANSPOSITION AND IMPLEMENTATION OF THE TISSUES AND CELLS DIRECTIVE

As a general point, the Competent Authorities remarked that they receive many questionnaires either from the Commission or from various organisations. From now on, the questionnaires or requests developed by the Commission on reporting in accordance

with legal provisions or necessary to monitor the implementation and transposition process will be called "Report templates". They are intended to facilitate reporting by the Member States.

3.1. Status of transpositions

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 transposition of the Directives.

In order to adequately monitor the transposition of the Tissues and Cells Directives, the Commission will prepare a "Report template: Transposition concordance table" that will be sent to Member States in autumn for completion.

3.2. Results of the 2009 Questionnaire on transposition and implementation of the Tissues and Cells Directives

The 2009 Questionnaire on transposition and implementation of the Tissues and Cells Directives was sent to Member States in March. The completion of the questionnaire fulfils Member States reporting obligations as laid down in Article 26(1) of Directive 2004/23/EC**.** The Commission presented a preliminary summary on findings based on answers sent prior to the meeting. 20 Member States had submitted replies online. It was agreed that outstanding submissions or eventual updates should be sent to the Commission by 15 June 2009.

3.3. Update of Implementation report of Tissues and Cells Directives

Article 26(3) of Directive 2004/23/EC provides that a report on the implementation of the requirements of the Directive, in particular as regards inspection and monitoring shall be transmitted to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions. The Commission explained to the delegations that the first report on implementation is in preparation and will be based on the answers given to the questionnaire referred to in point 3.2 and the outcome of the present meeting. A full draft should be ready at the end of June 2009. The Report should be finalised in October 2009.

3.4. Experiences of Member States during implementation

10 of the responding Member States declared having encountered difficulties during the implementation of the Directives. According to the answers to the questionnaire, the main problems and issues to be addressed by the Commission in the near future were related to the following:

(1) The particular requirements for accrediting/designating/authorising/licensing procurement organisations and tissue establishments solely distributing acellular material.

The Commission explained that acellular material is under the scope of the Tissues and Cells Directives.

(2) In the Medically Assisted Reproductive Technologies (MART) sector, some Member States questioned the provisions on timeframe and frequency of testing, in particular as regards the need to test the donor at the time of each particular donation.

The Commission took note of the comments.

(3) Problems in understanding the import/export requirements, in particular with regard to repeat testing and on how to deal with more stringent testing requirements in third countries.

The Commission explained that the state of play of the import/export instrument would be explained under point 4.5 of the agenda.

(4) Need for a permanent platform or network of tissues and cells inspectors.

The Commission explained that there is currently a Working Group on Inspection guidelines. Once the guidelines are adopted by Member States, meetings of this group could be convened based on specific needs.

(5) Inspections frequency requirements are considered to be excessive by some Member States (Article 7 of Directive 2004/23/EC requires inspections to be performed every two years).

The Commission explained that the draft Inspection guidelines address this issue.

(6) The wording of Directive 2006/86/EC concerning the air quality standards is according to some Member States open to interpretation, leading to implementation difficulties.

The Commission explained that currently the air quality standards as stated in point D. 3 of Annex I of Directive 2006/86/EC apply in conjunction with the flexibility provided by points D. 4 and 5. Further guidance could be discussed by the Competent Authorities based on the inputs provided by the concerned sectors.

(7) Problematic implementation of coding and traceability systems.

An update on the state of play for coding was given by the Commission: Currently an Impact Assessment is being launched.

(8) Need to inform further on the vigilance requirements.

The issue is being addressed through the Common approach document on reportable serious adverse events and reactions (see point 6.2).

(9) Specificities for the tissues and cells reproductive field.

The Commission explained that one of the aims of the questionnaire was to get specific insight of the MART field. The particularities of the sector are duly taken into account at the time each policy is developed.

4. INSPECTIONS

4.1. State of play for Inspection guidelines

The Commission made an update of the work carried out by the Working Group (WG) on Inspection guidelines formed by 16 experts nominated by the Member States. The Inspection guidelines are based on the Guidelines developed by the EUSTITE project (http://www.eustite.org/). The WG met twice this year (January and March) and is currently carrying out a final review of the Inspection guidelines. The final draft of Inspection guidelines will be sent to all Member States for a final revision at the end of July 2009.

The Commission explained that it was currently considering the possible legal form of the Inspection measures. One option could be a Commission Decision covering the core elements of the guidelines and approved by Comitology. The Commission Decision would be completed by detailed guidelines agreed by the Competent Authorities. Member States delegations supported this approach.

4.2. EUSTITE project: Presentation of the State of the art report

The work package leader (Ireland) made a presentation of the State of the art report, which corresponds to Work Package 5 of the EUSTITE project and was submitted to the Commission in January 2009. The report reviewed the activities carried out by the EUSTITE project (inspection guidelines and training for inspectors, vigilance and surveillance) and made a summary of major issues to be addressed in the future.

4.3. EUSTITE project: Training for inspectors

The work package leader (Austria) made a presentation of the currently on-going training for inspectors which corresponds to Work Package 7 of the EUSTITE project. So far 3 training courses have taken place, in total around 45 inspectors have been trained. The last training course will take place in Italy at the end of June 2009.

A final inspector training course design and supporting materials will be submitted to the Commission at the end of 2009.

4.4. Inspections of hospitals acting as Storage tissue establishments: French experience

France made a presentation on how they approach the accreditation/designation/authorisation/licensing and inspection of storage for end-use tissue establishments. France and most Member States have adopted a risk based approach in order to prioritise establishments to be inspected and accredited/designated/authorised/licensed.

At the beginning of the year, UK performed a survey among Member States in this respect and sent a summary table with the responses to all Member States and the Commission. From the responses received by UK, it seems that most of the responding countries do not expressly accreditate/designate/authorise/license storage for end-use tissue establishments.

Member States explained that a systematic accreditation/designation/authorisation/ licensing of storage for end-use tissue establishments would not be feasible, due to the large number of this type of establishments (ranging from hospitals to dentists).

The Commission will provide further clarification on the issue at the next meeting.

4.5. Import/export instrument: Inspections in third countries

The French and German delegations made presentations on their experience on inspections of third countries tissue establishments.

4.5.1. Import/export: State of play/EMEA collaboration

The Commission updated the participants on current issues regarding import/export from/to third countries. The draft Inspection guidelines address this matter in Annex 5 (Import/Export- Verification of technical requirements).

The EMEA has been consulted on the draft Inspection guidelines and has made some comments to Annex 5 which includes the criteria for conducting inspections in third countries. In this respect, the EMEA proposed to address the specific situation where tissues and cells are starting materials for the manufacture of advanced therapy medicinal products and an inspection or site visit is requested by the EMEA in connection with an application for a marketing authorisation or certification of the pre-clinical or quality data. Member States asked for clarification on who would be carrying out the inspection.

The possibility to perform joint inspections in third countries has been suggested by the Working Group on Inspection guidelines and has been inserted in Annex 5. The Commission explained that this should be coordinated by Member States. Competent Authorities expressed their concerns regarding the mechanisms on how to share information on inspection reports. It was agreed that further guidance on how to share the information is needed. This particular issue could be either addressed by the current or by future versions of the Inspection guidelines.

The Commission informed the delegations on findings derived from an on-going study on testing kits and testing laboratories authorisation and validation. The study addresses 5 Member States and 3 third countries. It will be finalised at the end of 2009.

5. UPDATE ON THE POSEIDON PROJECT

The project coordinator of POSEIDON (Promoting Optimisation, Safety, Experience sharing and quality Implementation for Donation Organisation and Networking in Unrelated haematopoietic Stem Cell Transplantation) presented the project. POSEIDON is a 3 year project that started in June 2008 and involves 8 partners. It aims at improving the safety of unrelated haematopoietic stem cell transplantation, optimising donation policy and promoting equal access to this therapy throughout the EU.

Some Member States were interested by the possibility of developing guidelines based on the findings of the project.

For more information, please go to: www.poseidon-hsct.eu/.

6. VIGILANCE

The Commission and the French delegation gave an update on the quick alerts issued during 2008. The Commission expressed the need for improvement of the current e-mail system used for spreading the quick alerts.

6.1. Proposal for a quick alert system

Denmark presented their reflections on an EU quick alert system. It was agreed that this document complemented by elements from other vigilance/surveillance tools, e.g. RASFF (Rapid Alert System for Food and Feed) model, would be circulated in June 2009 to the Competent Authorities for their comments by the 31st August 2009. A version compiling suggestions and comments should be discussed during the next Competent Authorities meeting.

6.2. Reporting systems on serious adverse reactions and events: Annual report 2009.

According to Article 7 of Directive 2006/86/EC Member States shall submit to the Commission an annual report on the notification of serious adverse events and reactions. The Commission presented the next (second) vigilance reporting campaign. The data received from Member States in 2008, referring to the data collected by Member States from September to December 2007, showed that some guidance is still needed in order to receive comparable and exploitable data. A draft Common approach document, developed jointly by the Commission with a group of Member States experts, was presented. The aim of this supporting document is to ensure that Member States are clear on what should be reported. Member States will receive the electronic "Report template on Serious Adverse Events and Reactions on Tissues and Cells" and the final version of the Common approach document in June 2009.

The Commission will make a summary report in November 2009. The Common approach document may be revised in 2010 in the light of experience.

6.3. Update of EUSTITE project – Vigilance and surveillance

The Work Package leader (Italy) presented the Vigilance and Surveillance part of the EUSTITE project which corresponds to Work Package 4. The aim of the WP is to develop a model for the reporting and investigation of adverse events and reactions associated with the quality and safety of tissues and cells in the EU. A reporting pilot phase is currently being tested (July 2008-July 2009) by the project.

A final report on surveillance systems will be submitted to the Commission at the end of 2009.

The Common approach document referred to in point 6.2. has integrated some of the tools developed by this Work Package of EUSTITE project.

6.4. Register of Tissue establishments and activity reports

Italy made an update on the current activities performed by EUROCET (European Registry for Organs, Tissues and Cells) and on the data collected.

The Commission encouraged the use of this portal as a way to fulfil the obligations of the Tissues and Cells Directives.

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

7. UPDATE ON ADVANCED THERAPIES MEDICINAL PRODUCTS REGULATION

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

Some Member States felt that the borderline between Tissues and Cells and Advanced Therapies Medicinal Products still needed further refinement. The Commission clarified that tissues and cells intended to be used for the manufacturing of advanced therapies medicinal products are covered by the Tissues and Cells Directives as far as donation, procurement and testing are concerned; this applies also to SAR/E occurring during or related to the mentioned steps.

8. UPDATE ON GOOD TISSUE PRACTICES -GTPS PROJECT

The project coordinator presented the state of play of the GTPs project, which aims at developing guidance on Good tissue practices regarding recovery, processing and preservation of tissues. The project addresses in particular ocular, cardiovascular, musculoskeletal, skin and other tissues. The second goal of the project is to develop related training guidelines for tissue establishments' personnel. GTPs is a 3 year project that started in June 2008 and involves 11 partners.

The project could in particular help in providing some inputs regarding the required standards for air quality for the processing of certain types of tissues and cells.

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

9. OTHER BUSINESS

9.1. Regulatory forum[1]

9.1.1. Pancreatic islets

The Commission receives recurrent questions on whether pancreatic islets are covered by the Tissues and Cells Directive, the Advanced Therapies Regulation or whether they should be classified as organs.

It was agreed that, without prejudice to an eventual future opinion of the CAT (Committee on Advanced Therapies), pancreatic islets, as far as they are used for the same initial function and as far as they are not substantially manipulated (for instance cultured), should be considered under the scope of the Tissues and Cells Directives.

9.1.2. Reporting obligations (Art. 10(1) of Directive 2004/23/EC)

[1] It should be noted that ultimately it is for the Court of Justice to provide conclusive interpretation of the Community law.

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.

Around 10 Member States follow this approach.

The Commission will check the legal validity of this approach. Further guidance will be provided during the next Competent Authorities meeting.

9.1.3. NAT/Syphilis: need to retest samples

Point 2.5.b) of Annex II of Directive 2006/17/EC provides that "Where tissues and cells of allogeneic living donors can be stored for long periods, repeat sampling and testing is required after an interval of 180 days.". Point 2.6 of the same Annex specifies that "If in a living donor (except bone marrow stem-cell and peripheral blood stem-cell donors) the 'donation sample' is additionally tested by the nucleic acid amplification technique (NAT) for HIV, HBV and HCV, testing of a repeat blood sample is not required".

It was agreed that no repeat testing for syphilis after 180 days should be necessary when point 2.6 of annex II of Directive 2006/17/EC applies, as contrarily to HIV, HBV and HCV, Syphilis is not a donation exclusion criterion as such.

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The next Competent Authorities meeting was provisionally set for October 2009.

Patricia BRUNKO