EUROPEAN COMMISSION
HEALTH & CONSUMERS DIRECTORATE-GENERAL

Directorate C - Public Health and Risk Assessment
C6 - Health Law and International

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Meeting of Competent Authorities

On Tissues and Cells

29-30 May 2008

Summary report

The second meeting of competent authorities on tissues and cells was convened on 29 and 30 May 2008 under the Chairmanship of Mr Tapani PIHA, Head of Unit, SANCO C6.

All Member States except Luxembourg were present at the meeting; were also present: Iceland, Liechtenstein, Norway, Switzerland, Croatia, Former Yugoslav Republic of Macedonia, Turkey, the Council of Europe, the US Food and Drug Administration and the EMEA. (List of representatives appended in annex I)

1. WELCOME AND INTRODUCTORY REMARKS BY THE CHAIRMAN OF THE COMMITTEE

The Chairman welcomed the delegations. The aim of the meeting was to discuss the progresses and difficulties encountered in the transposition and implementation of the Tissues and Cells Directive in the Member States, to have a discussion on a number of proposals by the Commission related to the implementation of the Tissues and Cells Directive, and to share information on programmes and initiatives in and outside the EU related to tissues and cells transplantation.

2. ADOPTION OF THE AGENDA

The agenda was adopted without change.

3. PRESENTATION OF THE DELEGATIONS

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

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4. GENERAL DISCUSSION ON THE TRANSPOSITION OF THE TISSUES AND CELLS DIRECTIVE

The Commission presented the findings of the questionnaire on the transposition and implementation of Directive 2004/23/EC which all National delegations except 2 have replied to.

4.1. Status of transpositions

The Commission presented the latest data regarding transposition of the T&C Directive. 76% of the Member States have completely transposed the Directive 2004/23/EC, 61% for the Directive 2006/17/EC and 48% for the Directive 2006/86/EC. The Commission has sent, or is about to send, letters of formal notice to 8 Member States for non transposition of the Directive 2004/23/EC, to 10 Member States regarding the Directive 2006/17/EC, and to 9 Member States regarding the Directive 2006/86/EC.

(Post meeting note: see press release at:
http://ec.europa.eu/dgs/health_consumer/dyna/enews/enews.cfm?al_id=751)

4.2. Results of the questionnaire

The Commission thanked the delegations for their contribution to the questionnaire. A preliminary analysis based on the answers sent prior to the meeting was presented to the Competent Authorities. The information needs to be further refined and will be compiled in a report that will be made available on the SANCO website.

4.3. Experiences of Member States during transposition

39 % of the responding delegations declared having difficulties for transposition of the Directive. Main problems related to time constraint, lack of resources, political debates around ethical issues (in particular in the reproductive medicines field) and competitive priorities in the legislative process and organisational changes.

65% of the responding delegations declared having difficulties for implementation of the Directive. Main problems highlighted related to time constraint, guidance on coding and establishing vigilance systems and inspection capacities. Some delegation stressed the need for cooperation at EU level, especially with regard to inspections.

Several issues were flagged by the delegations to be addressed rapidly: clarification of the interface between the T&C, the pharmaceutical and the medical devices fields; specificities of ART such the air quality requirements; guidance on coding and other IT solutions to meet reporting requirements; and addressing the authorisation of testing laboratories. Some technical clarification were also mentioned such the need for blood sampling after 24 hours..

Lack of frequent forum for all competent authorities to exchange views and practices was regretted by several delegations.

The Commission will explore all these issues to clarify them, it will continue also through an active cooperation with DG ENTR and other services to ensure coordination between the different fields.

5. REPRODUCTIVE MEDICINE

General discussion to exchange experiences on how Member States are addressing the field of reproductive medicine in relation to transposing the Tissues and Cells Directive.

Nine Member States described the organisational changes having taken place (or being on the way) in order to address reproductive medicine in the context of Tissues and cells Directive.

Dr Angela McNab introduced the European Assisted Conception Consortium (EACC) and explained that this group had been established to support the awareness and implementation of the Tissue and Cells Directive across member states in the area of reproductive health. The membership overall allowed three representatives from each member state: one clinician, one scientist and one regulator.

One of the key issues has been interpretation of the Directive specifically for reproductive health. A number of "hotspots" or areas of inconsistent interpretation have been identified. Dr. McNab presented these key areas which included:

Testing /screening arrangements, third party agreements, inclusion of embryos in the scope of the Directive, definition of "process", inclusion of IUI in the scope for the Directive, and arrangements for clinic closure. Many member states are anxious that if one state interprets the Directive less widely/strictly than another then it will make transportation from one state to another of embryos very difficult.

There was discussion on the issues and it was agreed that a subgroup might get together to manage them. Regulatory authorities were also encouraged to engage with the EACC and to support communication.

In parallel, the Commission will contact the Joint Research Center (JRC) to consider the possibility of undertaking a broad survey on the situation of reproductive medicines in the Member States.

6. UPDATE ON ONGOING ACTIVITIES

6.1. Working group on voluntary and unpaid donation: next steps

The Commission gave an update of the work carried out by the working group on voluntary and unpaid donation. A draft questionnaire has been developed, which will be refined and finalised after summer. The activities of the working group will continue during the second half of 2008.

6.2. Training course on tissues and cells

The Commission will organise a training course on tissues and cells banking in Brussels in October 2008. This training is funded under TAIEX (http://taiex.ec.europa.eu) and open to candidate and neighbouring countries. It is based on the training material and methodology developed by the EU co-funded project EQSTB. DG SANCO is exploring the possibilities to fund the participation of all EU Member States, An announcement of the course will be sent shortly to all CAs.

End of day one

7. REPORT ON THE EUROPEAN CODING SYSTEM: EXCHANGE OF VIEWS

Article 25 of Directive 2004/23/EC and article 10 of Commission Directive 2006/86/EC provides that a European coding system should be set to ensure proper identification, description and traceability of any donated material within the EU.

The European Commission has requested the CEN (European Standardisation Committee – www.cen.eu) to elaborate a technical recommendation on the shape and management of the European coding system. The CEN has set up a workshop in April 2007 (http://www.cen.eu/cenorm/sectors/sectors/isss/activity/tissues_and_cells.asp), open to all the authorities and stakeholders in the field, which reached its conclusions in May 2008. The CEN workshop agreement has been presented to the Competent Authorities by Dr. Esteve Trias, member of the CEN expert team that drafted the recommendation.

The Commission mapped the next steps of the elaboration of the European coding system: guidelines will be drafted in cooperation with the member states on the ground of the CEN recommendation. The guidelines will be adopted through comitology in 2009.

The Member States had an exchange of views on the issue. Overall they welcomed the work undertaken by and the conclusions of the CEN workshop as a critical step in the development of European guidelines which take advantage of the coding and traceability systems already operational in the Member States and worldwide.

8. REGISTERS OF TISSUE ESTABLISHMENTS AND ACTIVITY REPORTS

Article 10 of Directive 2004/23/EC requires that Tissue establishments shall keep a record of their activities. They shall submit to the competent authority or authorities an annual report on these activities. This report shall be publicly accessible. 52 % of the MS responded to the questionnaire that they have produced the annual report.

The same Article also provides that the competent authority or authorities shall establish and maintain a publicly accessible register of tissue establishments. 82 % of the MS maintain already such register. The Commission and MS have the obligation of link the different registers and make them publicly accessible.

EUROCET (European Registry for Organs, Tissues and Cells) is a project funded under the e-TEN programme of the European Commission, DG INFSO, aiming at setting up a registry on tissue and cell donation and transplantation activity shared by old and new Member States. Ms Caterina Delvecchio, of the Italian National Transplant Centre (EUROCET project manager) presented how the project has evolved during the last year to become a European platform collecting the activity annual reports and tissue establishment registries of the 27 EU Member States.

The Commission encouraged the use of this portal as a way to fulfil the requirements of the tissues and cells Directive.

9. REPORTING SYSTEMS ON SERIOUS ADVERSE REACTIONS AND EVENTS: ANNUAL REPORT.

1) Article 7 of Directive 2006/86/EC establishes that Member States shall submit to the Commission an annual report, by 30 June of the following year, on the notification of serious adverse reactions and events received by the competent authority. 2008 will be the first reporting year, covering the period between September to December 2007.

The Commission announced that a reporting pdf-form will be ready by early July. Member States were invited to use this format, with an extension of deadline to 15 July. UK and The Netherlands volunteered to test it before sending to all CAs. Those MS that would prefer to use their own reporting format this year are also entitled to do so.

2) The EU funded project 'European Union Standards and Training for the Inspection of Tissue Establishments' (www.eustite.org) has elaborated a preliminary model for the reporting and investigation of adverse events and reactions associated with the quality and safety of tissues and cells in the EU.

Dr. Deirdre Fehily of the Italian National Transplant Centre (EUSTITE Project leader) reminded the meeting participants that the EUSTITE project has 2 major streams of activity: one relates to inspection guidance and training and the other to vigilance and surveillance of tissues and cells. The vigilance and surveillance component has involved the development of a set of tools and guidance for this area.

Dr Fehily demonstrated the application of the tools using a series of examples of SAE/R in tissues and cells. These tools will be tested in a pilot programme that will run from July 1st 2008 to June 30th 2009 and will involve application of the tools, at least at the level of the CA, to all SAE/R reported in the period. All CAs from all MS and from EEA and applicant countries were invited to participate in this pilot by sending a message to **info@eustite.org**. Following the pilot, a final set of recommendations will be submitted to the European Commission.

10. INSPECTION SYSTEMS

Article 7 of Directive 2004/23 establishes the need for Inspections and control measures. It also requires that guidelines concerning the conditions of the inspections and control measures, and on the training and qualification of the officials involved in order to reach a consistent level of competence and performance, shall be established by Comitology.

Dr Johan Kurtz (Work package leader) presented an overview of the EUSTITE project part related to the drafting of the inspection guideline and the elaboration of the inspection training course.

The drafting group of the inspection guide studied internationally existing guidances on inspection, training and certification, compiled and tailored for the purpose of EU procurement and tissue establishment inspectors. Edition I and Edition II drafts were forwarded for open consultation. Hundreds of comments were incorporated in the document which then was submitted to the Commission as one of the deliverables of the project. The Commission will start now the internal procedure for adopting these documents through the comitology procedure.

The EUSTITE Project will run 4 inspector training courses during 2008/9 for tissue and cell inspectors. Each course has places for 15 participants who can be experienced inspectors or inspectors in training. All travel and accommodation costs will be paid by the project and there is no course fee.

Competent authorities should nominate trainees up to two weeks before the start of an e-learning module. Nomination form should be requested from **info@eustite.org**

11. UPDATE OF THE COMMISSION ON QUALITY SYSTEM: CALL FOR TENDER

The consultancy company Alcimed (www.alcimed.com) are conducting, on behalf of the European Commission, the one year project 'Proposition of a quality system guide in the field of substances of human origin'. The presentation introduced the project to the competent authorities, and covered the aims, methodology and progress of this project as it reaches the halfway point.

The involvement of the competent authorities and establishments of the member states was underlined as a key factor in the development of this proposition as it aims to help establishments across Europe to implement the sections of the blood and tissues and cells directives that relate to quality systems.

12. IMPORT AND EXPORT OF TISSUES AND CELLS

Article 9 of Directive 2004/13/EC regulates import and exports of tissues and cells from/to third countries. Article 9.4 provides that the procedures for verifying the equivalent standards of quality and safety of imported tissues and cells shall be established by the Commission, in accordance with the comitology procedure.

The Commission presented a working paper proposing different types of mechanisms to verify such standards equivalency.

The Commission provided details on a call for tender under the public health programme concerning an analysis and comparison of testing methods and testing laboratories in the EU and third countries.

Dr Ineke Slaper-Cortenbach (FACT-JACIE) presented the specificities of the cellular therapy sector regarding import and export issues. She introduced to the participants the latest recommendations of the Alliance for Harmonisation of Cellular Therapy Accreditation (AHCTA – regrouping actors in bone marrow, peripheral blood and cord blood based cellular therapies) regarding import and export of Haemopoïetic Stem Cells and related cellular therapies.

An exchange of views between the CAs took place on the added value of the potential initiatives in this field. Some Member States emphasized the need to focus on the implementation of the T&C Directive within the EU first before considering third countries involvement. However, it was acknowledged that it would be concerning to leave the Tissues Establishments without guidance in managing this growing part of their activity.

The United Kingdom has already developed import/export guidelines that they agreed to share with the participants.

The Commission invited the Member States to send their comments in writing on the proposed elements by 15 September.

13. OTHER BUSINESS

13.1. Open consultation launched by DG ENTR

The Commission informed about the posting on the "medical devices" website of DG ENTERPRISE of a 'Public Consultation on a Recast of the Medical Devices Directives' by (http://ec.europa.eu/enterprise/medical_devices/consult_recast_2008_en.htm). They were trying to assess, among other issues, the opportunity of broadening the medical devices legislation to cover medical devices that consist of, or which incorporate, non-viable human cells and tissues.

In particular stakeholders were invited to comment on an extension of the scope of the Directives, in particular, to include medical devices consisting of non-viable human cells and/or tissues and/or their derivatives and devices incorporating such cells and/or tissues and/or their derivatives with an ancillary action to that of the medical device;

This consultation was open until the 2nd July 2008.

13.2. Amniotic membrane: regulatory classification.

The Italian delegation informed that many Competent Authorities are finding difficulty with the inclusion of some 'tissues and cells for non-homologous use' in the Advanced Therapy Regulation. In particular the use of amniotic membrane in the eye could be classified as a medical product, subject to market approval.

Many of the EU tissue banks regulated under Directive 2004/23/EC procure process, store and supply this tissue for ocular use. If this is to be considered a medicinal product, CAs are concerned that the service from which many patients currently benefit might not be available to patients in future.

The delegations agreed that the processing is completely equivalent to other tissues in terms of complexity and scale. This use can be considered as homologous because the function it performs is the same whether on the placenta or on the eye (same essential functions). This coincides with the position taken by the FDA.

The representative of the EMEA recognised that the agency has not taken any scientific opinion on this issue. Acknowledging that this group is not competent to produce any regulatory decision on the classification of this type of tissue, there was a unanimous consensus between the CAs to consider the use of amniotic membrane for cornea replacement as homologous, and therefore in the scope of Directive 2004/23/EC.

Tapani PIHA

Chairman of the Committee

ANNEX I

List of Participants

Member States	
BE **Belgique / België**	**Federal Agency for Medicines and Health Products**
BG **Bulgaria**	**Executive Agency for Transplantation**
CZ **Česká Republika**	**Ministry of Health**
DK **Danmark**	**Danish Medicines Agency** **National Board of Health**
DE **Deutschland**	**Bundesministerium für Gesundheit** **Paul-Ehrlich-Institut**
EE **Eesti**	**Ministry of Social Affairs**
EL **Elláda**	**Institute of Biomedical research Foundation, National Transplant Organization** **Human tissue bank, National Centre for Scientific research "DEMOCRITOS"**
ES **España**	**Organización Nacional de Trasplantes**
FR **France**	**Ministère de la Santé** **Agence de la Biomédecine** **Agence française de sécurité sanitaire des produits de santé**
IE **Ireland**	**Irish Medicines Board**
IT **Italia**	**National Transplant Centre (Centro Nazionale Trapianti (EUROCET))** **Registro Nazionale della Procreazione Medicalemente Assistita, Istituto Superiore di Sanità**
CY **Kypros**	**Ministry of Health**
LV **Latvija**	**Ministry of Health** **Health Statistics and Medical Technologies State Agency**
LT	**National Bureau on Transplantation**

Lietuva	
HU **Magyarország**	**Department of Public Health, National Chief Medical Officer's Office (NPHMOS)**
MT **Malta**	**Ministry of Health, the Elderly & Community Care**
NL **Nederland**	**Ministry of Health, Welfare and Sport** **Department of immunology, The Utrecht centre for Gene and Cell Therapy**
AT **Österreich**	**Bundesministerium fur Gesundheit und Frauen** **Institut Medizinproducte und Haemovigilantz**
PL **Polska**	**Director of the National Centre of Tissues and Cell Banking**
PT **Portugal**	**Autoridade para os Serviços de Sangue e Transplantação**
RO **Romania**	**Agencie Nationale du Transplant** **Ministry of Health**
SI **Slovenija**	**Ministry of the Republic of Slovenia, Directorate of Health Care** **Agency for Medicinal Products and Medical Devies** **Institute of Transplantation of Organs and Tissues of the Republic of Slovenija**
SK **Slovensko**	**Ministry of Health**
FI **Suomi/Finland**	**National Agency for Medicines**
SE **Sverige**	**National Board of Health and Welfare** **Medical Products Agency**
UK **United Kingdom**	**Human Tissues Authority** **Human Fertilisation and Embryology Authority** **Ministry of Health, Public Health Delivery**

EFTA Countries	
IS **Ísland**	**Ministry of Health and Social Security**
LI **Lichtenstein**	**Ministry of Health**
NO **Norge**	**Norwegian Directorate for Health**
CH **Swiss Confederation**	**Federal Office for Public Health**

Candidate Countries	
HR Hrvatska	**Ministry of Health and Social Welfare**
MK poranešna jugoslovenska Republika Makedonija	**Clinic for Gynecology and Obstretics**
TR Türkiye	**Directorate General for Treatment Services – Ministry of Health**

Observers	
	EFTA Secreteriat
	EDQM Council of Europe
	CBER/FDA
	WHO
	ALCIMED
	EMEA
	PHEA
	CEN
	EUROCET