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Meeting of the Competent Authorities for Tissues and Cells

23 - 24 June 2011

Summary Report

The meeting of the Competent Authorities on Tissues and Cells was convened on 23 and 24 June 2011. The previous meeting of National Competent Authorities (NCAs) took place in 6 and 7 December 2010.

PARTICIPATION:

All Member States except Bulgaria and Romania were present at the meeting of the Competent Authorities (CA) on 23 and 24 June. Liechtenstein, Norway and Croatia, as well as the European Directorate for the Quality of Medicines and Health Care of the Council of Europe (EDQM) and the European Centre for Disease Prevention and Control (ECDC) also attended the meeting.

Commission:

Chairman: Mr Antti MAUNU (SANCO)

Ms I. SISKA, Ms H. LE BORGNE, Mr. Stefaan VAN DER SPIEGEL (SANCO D4)

1. ADOPTION OF THE AGENDA

The agenda was adopted without changes.

2. SURVEILLANCE AND VIGILANCE

2.1. Update on infectious disease risks: latest news (ECDC and Member States)

2.1.1. Q-fever

ECDC briefly presented the recent changes in its structure due to the recent reorganisation of the agency. It was mentioned that no changes of mandate were operated.

Following the outbreaks of Q fever which affected some of the MS in the last years, ECDC gave an update on the current epidemiological situations and needs of safety measures.

ECDC's presentation showed that since the beginning of 2011, low incidence rates have been reported in Germany and Netherlands. Outbreaks in Germany in January/February 2011 were not related to the outbreak in the Netherlands. ECDC concluded that based on the available data for 2011, the risk for collecting contaminated blood donations in the Netherlands, as well as the risk for donors from other EU Member States after travel to the Netherlands has considerably decreased, compared to 2010, suggesting that Member States may want to take into account this change of estimated risk in their safety assessments.

NL representative gave an overview of the situation concerning Q fever and its implications on the supply of tissue, cells, blood and blood products in 2011. Currently, because there are no risk areas, there are no special recommendations to be made to the NCAs group.

Following both ECDC's assessment and NL report, the Competent Authorities from BE and AT stated that they are waiting scientific advice also from national experts, but most probably will discontinue the Q fever-related safety measures taken last year.

2.1.2. West Nile Virus

Following the decision of the Blood NCAs in October 2010 to set up a subgroup of Competent Authorities to develop a European preparedness plan for the anticipated outbreak of West Nile Virus in 2011, ECDC co-organised with DG SANCO and the Greek Competent Authority a workshop in Thessaloniki in January 2011. This work was led by Greece, in close cooperation with several Competent Authorities (IT, FR, RO), ECDC and the European Blood Alliance (EBA).

ECDC briefly introduced the workshop and some of its key-outcomes. Elements covered include the definition of "affected area", need for real-time sharing of epidemiological overview at EU level for decision making in other EU countries, strengthening surveillance in at-risk and affected countries, further need for guidance on how to apply EU blood directive.

It was mentioned that the preparedness plan will be finalized by July 2011 and that ECDC will provide the models and relevant data for risk assessment and that a coordinated tool will be available by the ECDC at the beginning of summer 2011.

Member States in general found the Commission communication to the Competent Authorities on the WNV very useful. It was agreed that DG SANCO will circulate also to the Competent Authorities for Tissues and Cells the updated preparedness plan, together with the link to regularly updated maps of Europe with WNV cases provided by ECDC.

2.1.3. Other

Member States did not report any additional information on infectious diseases.

ECDC informed about the outbreak of Shiga-toxin producing *E. coli* (STEC) in Germany. It was appreciated as very unlikely that this E.coli strain would be able to infect the blood or release significant toxin into the blood of a healthy person in the asymptomatic incubation phase of the disease, therefore ECDC concluded that the risk for blood and tissue donation was considered negligible.

2.2. Serious adverse reactions and events: Preparation for the 2010 Annual report

Article 7 of Directive 2006/86/EC requires that Member States shall report serious adverse events and reactions every year to the Commission.

The Commission announced that the third round of the annual report template on serious adverse events and reactions (2010 data) will shortly be sent out to the Member States. It was agreed that Member States should report the data to the Commission by 31 August 2011. Member States supported the proposal for a short, anonymized quality check as soon as replies come in, allowing for corrections in case of format/interpretation issues.

Member States were also invited to send to the Commission their remarks and problems they encountered in relation to the 2011 collection and reporting of data (2010 data). This input will serve as basis for the major update before the 2012 exercise and will be forwarded to the SOHO V&S project, which should tackle this work under Work Package 7.

2.3. Update on the development of a European support for Tissues and Cells

2.3.1. Information on the output of the last meeting of Working Group on coding of tissues and cells (31/01-01/02/2011)

The technical progress of the Coding Working Group was presented to the Competent Authorities. The objective is to develop a simple system that is as compatible as possible to the different systems and situations in the Member States.

The Working Group's work has lead to a proposal for structure to be put on the label:

Donation identification:

ISO country	TE code	Unique donation number (local/national)
2 characters	6 characters (alpha-numeric)	13 characters (alpha-numeric)

Product identification

Product code	Split number	Expiry date
1symbol + 7 characters (alpha-numeric)	3 characters (numbers)	8 characters (numbers)

The Working Group considered that such structure would allow Member States to use inputs from ISBT128, Eurocode, as well as from other systems.

The Working Group had discussed with representatives of European Association of Tissue Banks (EATB), European Society of Human Reproduction and Embryology (ESHRE) and Worldwide Network for Blood & Marrow Transplantation (WBMT), which provided for tissue-specific comments and are to be taken into account for further developments. It was clarified that partner donation of reproductive cells will not be subject to this coding system.

During the following discussion some technical concerns were expressed. The Commission ensured that they will be taken into account during the further European coding system development. At the end of discussion the Competent Authorities expressed unanimous support for this structure and asked the Commission and Working Group to move to the next steps.

The Competent Authorities were informed that the Commission plans to contract external service providers to help implement the coding system (a compendium with tissue establishments for donation nomenclature and a compendium with product nomenclature). Some historical concerns were expressed regarding involvement of potential service providers. However it was clarified that service providers will only be involved upon the conditions and request of the Commission and the needs defined by the Working Group.

The Commission was asked to inform professional associations of the structure supported by the competent authorities and the plans for next steps.

The Competent Authorities congratulated the members of the Working Group for their work.

2.3.2. Information on developments for establishment of a European support for tissues and cells – governance issues

The Commission explained the activities in order to involve a European Agency (ECDC/EMA) in the set-up and running of the EU vigilance and traceability support for tissues and cells. A document with EU level support tasks and the involvement of EMA and ECDC services has been prepared and agreed upon by the EMA and ECDC Management Boards.

Some concerns were expressed regarding the need to clearly distinguish tissues and cells from pharmaceutical products and to organise vigilance and traceability for both in an efficient and complementary way.

The concrete set-up and involvement of the 2 agencies is to be presented to a Steering Group involving some members of the EMA and ECDC Management Boards, as well

as some members of the Competent Authorities for Tissues and Cells. The Commission will ask Competent Authorities to express their interest to attend the Steering Group meetings, without confirming that all interested NCAs will be invited, given that overall membership of the Steering Group is to be geographically balanced with the candidate members of the EMA and ECDC Management Board.

The Competent Authorities urged for progress and reminded that several national systems are waiting for progress at EU level.

3. INTERPRETATION QUESTIONS

3.1 Cornea donation in relation to the 24-hour requirement for blood sampling – update

Article 4 and Annex II of Directive 2006/17/EC (implementing measure of Directive 2004/23/EC on tissues and cells) set the testing requirements for donors of tissues and cells. Annex II point 2.4 specifies that, "in the case of a deceased donor, blood samples must have been obtained just prior to death or, if not possible, as soon as possible after death and in any case within 24 hours after death".

The issue of the 24 hours testing requirement was initially discussed with Member States Competent Authorities for tissues and cells during the meeting on 20-21 May 2010 following an enquiry from the University Medical Centre of Freiburg (Germany). Most Member States informed that they had not encountered problems of increase in cornea loss because of the testing requirements in Article 4 and Annex II of Directive 2006/17/EC. In addition many MS expressed the view that serological viral testing within 24 hours after donor's death is feasible, necessary and appropriate.

This matter was discussed again during the Competent Authorities meeting held on 23-24 June 2011 when the Swedish Competent Authority presented the preliminary results of a national study which noted that the availability of cadaver corneas in Sweden may be reduced by over 60% due to the 24-hour limit for post mortal blood sampling. A study of the Charité hospital in Berlin was also quoted. The Group of Competent Authorities considered that further validation of assays and data is required, as well as an improved statistical analysis.

The Member States Competent Authorities for tissues and cells concluded that to date there is not sufficient scientific evidence submitted to support a change in testing requirements set by the Annex II of Directive 2006/17/EC. It was also mentioned that cornea donation rate largely depends upon an appropriate organisational set-up, as proved by the excellent results obtained by several Member States (IT, DK, PL, PT).

In the light of new relevant and validated scientific evidence the Commission may bring again the issue for discussion with the Member States Competent Authorities for tissues and cells and if necessary seek scientific advice.

3.2. Follow up HTLV I/II testing requirements

The Directive 2006/17/EC, Annex II and III require HTLV-I antibody testing for donors living in / originating from high-incidence areas or with sexual partners originating from those areas or where the donor's parents originate from those areas.

In 2010, the American Association of Tissue Banks (AATB) agreed to align with FDA's line not to impose an HTLV test for tissues with an absence of viable leukocytes e.g. corneas and highly processed tissue. Following a recommendation by the Regulatory Committee on T&C, EC asked ECDC to assess the possible risks of the change in HTLV testing for human tissues and cells imported from USA into the EU.

During the last NCAs meeting in December 2010, ECDC presented the draft risk assessment on HTLV transmission by tissue/cell transplantation. At that moment in time, it was agreed that the final report will be analysed by a WG consisting of UK, IT, DE, FR and ES to discuss possible ways forward with regard to HTLV testing requirements in the EU legislation, the work being co-ordinated by the UK and DG SANCO.

The conclusions of the HTLV Working Group were presented by the UK Competent Authority. Three approaches were suggested: 1) Amend Annex II and III of the Directive 2006/17/EC by changing from high "incidence" to high "prevalence"; 2) Initiate a six month project to obtain accurate HTLV testing data throughout all EU MSs, in order to establish overall infection rates and prevalence and identify sub-populations with high prevalence; 3) Establish a consistent approach to testing.

The group of the Competent Authorities concluded that changing from high "incidence" to high "prevalence" should be operated when the Directive will be revised. In the meantime, the group agreed upon an action to improve data collection on HTLV testing, with the following steps: 1) all MS who did not yet provide data were asked to send the requested information to UK Competent Authority (HTA); 2) based on HTLV prevalence data provided by MS from blood donors, as well as from other risk groups, ECDC could map the HTLV-high prevalence areas in EU; 3) upon analysis of the data collected in EU and HTLV prevalence data worldwide, the UK Competent Authority (HTA) should propose a list of high-prevalence geographical areas to be used by all EU Competent Authorities.

3.3. Interpretation of the EU legislation (Directive 2004/23/EC) regarding the Celution (manufactured by Cytori)

The Commission was asked whether the procurement of stem cells from autologous adipose tissue by Celution® and re-implantation within the same surgery process to the same patient is considered in or out of scope of the Cell & Tissue Directive 2004/23/EC. The device is currently used for reconstructive surgery (e.g. reconstruction of the breast following mastectomy).

The Commission briefly presented the main features of the Celution device, which is a CE-marked medical technology enabling real-time access to adipose-derived stem at the bedside. The device automates and standardizes the extraction, washing, and concentration of a patient's own adipose-derived regenerative cells (ADRCs), which

can then be redelivered to the same individual within the same surgery process in the same operating room (cells/tissues never leave the operating room).

Several Competent Authorities have expressed their opinions on the procedure (CZ, DK, SK, PT, IT).

Conclusively, the group of Competent Authorities for Tissues and Cells considered that that procurement of stem cells from adipose tissue using the above mentioned procedure, when used to the same individual within the same surgery process, in the same operating room, when cells used with the same essential function ((e.g. adipose-derived regenerative cells restoring the adipose mass of the breast following mastectomy for breast cancer), should be exempted from the Cell & Tissue Directive 2004/23/EC, based on Article 2.a.

4. INTERACTION WITH EUROPEAN MEDICINE AGENCY COMMITTEE FOR ADVANCED THERAPIES (CAT) ON BORDERLINE ISSUES BETWEEN TISSUES&CELLS AND ADVANCED THERAPIES MEDICINAL PRODUCTS (ATMPS)

The chairman of the Committee on Advanced Therapies (CAT) in EMA gave a presentation explaining the work of CAT and presenting the borderline areas/potential topics of overlap between the field of Tissues and Cells for transplantation and the field of Advanced Therapies Medicinal Products (ATMPs).

A constructive exchange of views followed and it was agreed that a WG will be organised to discuss such borderline issues and also to allow more interaction between CAT and T&C CAs in view of the new coding system at EU level. National Competent Authorities were asked to express their interest in writing to SANCO D4.

It was also agreed to give EMA CAT secretariat access to the tissues and cells CIRCA system and to collect all opinions on borderline issues agreed during previous meetings of tissues and cells NCAs.

5. INFO - REVISION OF THE MEDICAL DEVICES DIRECTIVE

A COM representative of the SANCO B2 (cosmetics and medical devices) introduced this topic. He provided information regarding the preparations for the revision of the regulatory framework for medical devices[1] scheduled for the 1st semester 2012. The impact assessment by SANCO B2 is ongoing and will be presented to the Commission's Impact Assessment Board by mid- or end of September 2011.

The meeting confirmed that as "next steps" it would be useful to (1) collect further examples of borderline products (i.e. those consisting of non-viable human material) and to indicate the current regulatory pathway; (2) develop a collaboration with the authorities in the field of medical devices for topics like vigilance or traceability.

It was also suggested that CAs on T&C get in contact with their national colleagues responsible for medical devices, to discuss this topic further.

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1 Directives 90/385/EEC, 93/42/EEC and 98/79/EC.

It was concluded that SANCO D4 would allow further written comments by the participants, that will be forwarded as input from T&C CAs meeting to SANCO B2 for consideration.

6. INFO - POTENTIAL EU FUNDING OPPORTUNITIES IN THE FIELD OF TRANSPLANTATION WITHIN THE 2012 HEALTH RESEARCH THEME OF THE EU-FUNDED 7TH FRAMEWORK PROGRAMME

The 2012 draft work-programme ("Orientation Paper") of the 7th Framework Programme - Health theme was published in May and includes some topics interesting for specialists in the field of transplantation, e.g: Health.2012.1.4-1: Innovative approaches to solid organ transplantation and Health 2012.1.4-2: Medical technology for transplantation and bio-artificial organs (http://ec.europa.eu/research/participants/portal/page/cooperation?callIdentifier=FP7-HEALTH-2012-INNOVATION-1).

The topics were presented by the Scientific Officer responsible for these topics from Directorate F – Health of DG RTD.

It was agreed that this opportunity may provide significant additional funding to enhance knowledge in this field of transplantation and national CAs may consider disseminating this information to colleagues who could be interested in submitting proposals for such topics.

7. ART: FEEDBACK FROM EXPERT GROUP MEETING ON TESTING REQUIREMENTS FOR PARTNER DONATION (NOT DIRECT USE)

As laid down in Annex III of Directive 2006/17/EC, donors of gametes, including partners (not for direct use), shall be subject to testing at the time of each donation (for HIV and Hepatitis B & C).

Following the discussion at the Competent Authority meeting of 19-20 October 2009 when some MS made a case that the current testing requirements are cumbersome and costly, and do not necessary add to the safety of human substances meeting, it was agreed to set up an expert working group to review and discuss the evidence base for testing requirements for partner donation of gametes (not for direct use), and a possible legal change of testing requirements. The WG included NCAs (DK, IE, BE) and ESHRE and has taken into account ECDC's risk assessment on change of testing requirements for reproductive cells in partner donation, as well as the experience and studies provided by the participating NCAs.

The NCAs group concluded that it was not needed to maintain the current testing requirements for partner donation as laid down in Annex III of Directive 2006/17/EC. This will require a future amendment of the Directive, through the regulatory procedure. It is the responsibility of the NCAs to ensure that ART tissue establishments have in place the appropriate safety and quality systems, which does not affect the safety and quality of reproductive cells and/or human health when donors are tested at up to 24 months time intervals.

However, NCAs also expressed regret for past public statements by stakeholders on this topic and re-emphasised the need for solid facts and data to allow for a constructive approach.

8. REPORT ON THE PROMOTION OF VOLUNTARY AND UNPAID DONATIONS (ARTICLE 12.1 OF DIRECTIVE 2004/23/EC)

In accordance with Directive 2004/23/EC, article 12, the Member States shall report on the practice of voluntary and unpaid donation of tissues and cells to the Commission every three years.

The Commission sent out a report template to the Competent Authorities for tissues and cells during the summer of 2010. A draft report with the main findings was presented to the Competent Authorities during the meeting in December 2010, when Member States were also asked them to provide comments until 15 January 2011.

The Commission presented the main findings of the recently published (17 June 2011) "2nd Report on voluntary and unpaid donation of tissues and cells" with the aim to discuss them with the Member States.

The Council of Europe mentioned that this topic is also tackled by the CD-P-TO group. The NCAs group confirmed its support for the work of the Council of Europe, and it was agreed that Commission and Council of Europe should continue collaboration on this topic.
FR Competent Authority suggested including in the next report data concerning public vs. private ART establishments procuring reproductive cells. IT Competent Authority suggested also collecting and incorporating data on compensation foresaw in EU Member States for donation of reproductive cells (separately for sperm and oocytes).

The issue of advertising was also discussed in relation to private cord blood banks, which in some cases provide misleading/incomplete information to potential customers. EC SANCO took notice of the above comments and will consider this issue as a topic for one of the next NCAs meeting.

The Competent Authorities agreed that the current legal text reflects well the different points of view within the EU and that no legal changes are needed. It was therefore concluded that no further measures are needed on voluntary and unpaid donation of tissues and cells at EU level.

9. UPDATE AND INFORMATION ON THE TRANSPOSITION AND IMPLEMENTATION OF THE TISSUES AND CELLS DIRECTIVES

Member States are under the legal requirement to transpose the directives into national law one year after adoption and the Commission has the duty to check the transpositions.

The Commission gave an update on the state-of-play concerning the transposition checks of the tissues and cells directives. The Commission explained the main areas that were identified in the directives as being important in the transposition checks.

Member States were informed that the new web-based tool developed by the Commission was finalised and was already tested with the help of 3 NCAs (FR, IE, UK); their feedback was used to improve some practicalities related to the online answering process.

The Commission announced that the web-based tool will be launched shortly and a letter will be sent out to the Member States with login and passwords for each NCA. It was agreed that Member States with more than one CA, will receive two logins and passwords, but they should coordinate in order to submit only one reply per Member State. The answers should be provided by 15 October 2011.

10. PROJECT PRESENTATIONS

10.1. SOHO V&S

The SOHO V&S project is funded by the 2nd Public Health Programme and it is coordinated by the IT Competent Authority, who updated the NCAs about the progress of several work-packages.

The project aims to support EU MS in the establishment of effective vigilance and surveillance systems for T&C used in transplantation and in assisted reproduction. The project will drive harmonisation in terminology, documentation and investigation approaches to improve communication and facilitate cross-border management of SARE associated with T&C donation or human application. The project should provide guidelines for MS that are setting up new V&S systems, T&C community-wide guidelines, as well as training programmes for their staff.

The work of several work-packages was presented.
Council of Europe referred to its work against illegal and fraudulent activities in the field of transplantation, for both organs and tissues and cells. Commission expressed its support to this work. It was also agreed that WP6 of the SOHO V&S project, can give a valuable input for the development of a new international instrument to fight against illegal and fraudulent activities as foreseen in the preliminary opinion expressed by the Council of Europe.

10.2. EUSTITE

EUSTITE was an EU funded project under the 1st Public Health Programme that finished in December 2009. It developed guidance and training courses for EU CAs on the inspection of TEs and on vigilance of T&C used in transplantation and in assisted reproduction. Some key outputs of EUSTITE were the project's Final Vigilance Recommendations and vigilance tools and a report of a one-year Vigilance Pilot in which 20 EU countries participated.

The AT Competent Authority in cooperation with FR Competent Authority provided a brief overview of the training programme developed by EUSTITE and continued with the AT support due to the increased requests coming from several MS.

11. AOB

11.1. Transplant activities in Bulgaria

The Competent Authorities for Tissues and Cells have expressed their concern regarding recent media coverage on problems in donation and transplantation activities of substances of human origin in Bulgaria. There was in particular reference to practices in egg cell donation, the limitation of the number of kidney and liver transplant centres, and the role of the Bulgarian transplant agency.

The Competent Authorities underlined that the efforts made in many Member States to promote donation and transplantation of human substances are highly dependent on a positive public perception, and this perception can be negatively impacted from messages like the ones in Bulgaria. They also highlighted that activities organised within one Member State of the EU can impact safety and quality for donors and recipients, in and from other EU Member States.

The Competent Authorities regretted the absence of the Bulgarian representative in this meeting, which would have allowed clarifying the situation and asked DG SANCO to request more information from the Bulgarian Ministry of Health regarding the above mentioned issues. The EU National Competent Authorities should be informed about the reply during the next meeting.

11. 2. Joint Conference & Workshop on human transplants identification and monitoring in European Union - Quality and Safety Standards Katowice, October 6-7, 2011

The PL representative invited all MS Competent Authorities for Tissues and Cells to attend a meeting organised by the Polish authorities to be held in Katowice on 6 and 7 October. The meeting aims to gather both Organs and Tissues&Cells Competent Authorities (2 representative per MS, one for organs and one for tissues and cells) to discuss quality and safety standards in the transplantation field in EU.

Antti Maunu