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Competent Authorities on Substances of Human Origin Expert Group (CASoHO E01718)

Meeting of the Competent Authorities for Tissues and Cells

3 - 4 June 2015

Summary Report

The meeting of the Competent Authorities on Tissues and Cells was convened on 3 and 4 June 2015. The previous meeting of Tissues and Cells National Competent Authorities (CAs) took place on 3 and 4 December 2014.

PARTICIPATION:

All Member States (MS) were represented at the meeting. In addition, Norway, the Former Yugoslav Republic of Macedonia and Turkey, as well as representatives of the Consumer, Health and Food Executive Agency (Chafea) and the European Centre for Disease Prevention and Control (ECDC) joined as observers.

European Commission (DG SANTE):

Chairs: Mr D. SCHNICHELS, Mr S. VAN DER SPIEGEL

Commission Representatives: Ms I. SISKA, Mr R. Mc GEEHAN, Mr P. CATALANI

Administrative Assistants: Ms A. CORNEA

1. WELCOME AND ADOPTION OF THE AGENDA

With the minor modifications of moving points 5 and 6 from day 2 to day 1, and point 2.6 from day 1 to day 2, the agenda was unanimously adopted. No conflicts of interest were reported.

2. LEGAL MATTERS

2.1. Update on the transposition of the Tissues and Cells Directives (COMM)

The Commission briefly updated the participants about the status of the transposition check and the on-going infringement proceedings and pilot procedures. It was reported that as of June 2015 the transposition check had been satisfactorily closed for eighteen Member States, there were five pilot procedures open, while a further three pilot procedures were expected. One Member State was the subject of formal infringement

proceedings with one of these having been referred to the Court with ruling expected for June 11.

Nota Bene: In its June 11 ruling the European Court of Justice declared that, by excluding reproductive cells and foetal and embryonic tissue from the scope of the provisions of national law transposing the directives at issue, the Republic of Poland had failed to fulfil its obligations under Article 31 of Directive 2004/23, under Articles 3(b), 4(2) and 7 of, and Annex III to, Directive 2006/17, and under Article 11 of Directive 2006/86. Poland must now act to rectify this situation.

Regarding the pilot procedures, the Commission clarified that these remained open due to a lack of reply from certain Member States, the replies were being translated or Member States had indicated that national legislation would be amended to take into account the points raised by the Commission. In such cases the Commission recalled the need to be informed when such amendments had been adopted.

2.2. Debrief from the joint meeting of Tissues and Cells Competent Authorities, National Competent Authorities for Human Medicinal Products and representatives of the Committee for Advanced Therapies (CAT) in EMA (COMM)

The Commission presented an overview of the discussions and conclusions of the joint meeting organised on 23 April 2015. Besides an overview of the respective legal frameworks (i.e. tissues and cells and ATMP), the following topics were addressed: borderline issues between the two areas, differences in national rules on donation, procurement and testing and their potential impact on the two sectors, availability of human tissues and cells based therapies and quality and safety requirements for starting materials for ATMPs. Due to time constraints, one topic was not discussed (i.e. exchange of rapid alerts between authorities in the two sectors) and there was only a short exchange of views on the issue of new devices used for providing cell-based therapies at bedside. The Commission informed attendees that draft minutes will be circulated for the participants' feedback in the following month.

During the group discussions, several CAs emphasised the importance of organising such meetings which allow for a direct interaction between tissue and cell CAs and CAT together with CAs for medicinal products. The group felt that this joint meeting had improved mutual understanding, whilst significant tensions became transparent. The DE representative highlighted the need to focus on commonalities between the tissue and cells and ATMP frameworks, in particular to make sure the tissue/cell based therapies are safe and function well.

Several CAs supported the idea of continuing the discussions started in April by creating working groups including representatives of both Competent Authorities and CAT. The group of the Tissues and Cells CAs identified four topics which may be addressed by such working groups:

- clarification of borderline issues and regular and early-on consultations on the status of (innovative) therapies;
- developing a common approach to authorise of tissue and cell preparation processes taking account, not just of safety and quality, but also of the assessment whether tissues/cells are (not) clinically (in)effective;
- application/comparison of GTP versus GMP rules;

- the understanding of the application of more strict safety and quality requirements per Member State (beyond the minimum criteria laid down in EU legislation).

The Commission was also asked to circulate the hyperlink to the new "Reflection paper on classification of advanced therapy medicinal products" drafted by CAT. The possibility to give input on such guidance documents elaborated by CAT, which also address or may have impact on the tissue and cell sector, was considered an essential part of future collaboration, and in the end for ensuring an appropriate implementation of (all) EU regulatory frameworks.

The Commission took note of all the above suggestions and will consult on next steps with the relevant Commission unit.

2.3. Interpretation questions

2.3.1. Regulation of lymphocyte immunotherapy (LIT) (COMM)

The topic of lymphocyte immune therapy (LIT) was first introduced by UK HTA during the CAs meeting in December 2014. Following the agreement to seek advice from its Legal Service, the Commission informed the group that Legal Service was consulted on three issues: whether withdrawal of whole blood leading to extraction of lymphocytes falls within the scope of blood or tissues and cells legislation, whether Member States may choose to regulate this activity under either their national blood or tissues and cells legislation and finally whether within a Member State, its authorities have the discretion to regulate the activity under both their national blood and tissues and cells legislation.

The Commission reminded the group that only the European Court of Justice can give legally-binding interpretations of Union legislation. After careful analysis of the situation put forward and the relevant legislation, the Commission put forward its working interpretation for the group's consideration. It was felt that justifiable arguments could be made for this activity falling under either the blood or tissues and cells legislation. This being the case, based on the specific nature of their national circumstances (assessment of risks to human health / desired level of human health protection / the existence of more stringent protective measures etc…), and given the fact that LIT is typically a local activity not involving cross-border steps, Member States benefit from a certain degree of discretion when deciding whether to classify this activity under either blood or tissues and cells legislation.

On the final point the Commission reminded the group of the importance of maintaining legal certainty within any given national legislative framework but did not exclude the possibility that in this specific case authorities within one Member State could allow the same activity to be governed under both sets of legislation, depending on the establishment which performs it, provided that this is justified by an assessment of the risks to human health and the desired level of protection specific to that Member State focusing in particular on largely equivalent levels of quality and safety assured under both sets of national legislation. The view of the Commission's Legal Service will be presented in the December meeting.

2.3.2. Compatibility of national laws with Union law in relation to the cross-border distribution of sperm to natural persons (COMM)

Following a request for clarification from the MS CAs, the Commission informed the group that the Commission Legal Service was asked whether a requirement to distribute sperm to an authorised tissue establishment or authorised organisation responsible for human application (i.e. a restriction on direct distribution to natural persons) is in line with Union law and if such a restriction is in line with Union law, can Member States with such restrictions in place require the cooperation of the MS of origin in enforcing them.

The Commission reminded the group that only the European Court of Justice can give legally-binding interpretations of Union legislation. After careful analysis of the situation put forward and the relevant legislation, the Commission put forward its working interpretation for the group's consideration. The Commission stated that not only would such a restriction be admissible in order to implement EU quality and safety standards, the lack of such a restriction may be regarded as not being in line with Union legislation and in particular the provisions on traceability and the obligation to report (serious) adverse reactions. In the discussions which followed the authorities from those countries principally affected by this situation indicated their willingness to cooperate on this issue with a view to examine the possibilities for such a national restriction.

2.4. Mapping by the Commission of the more stringent safety and quality requirements in the Member States (COMM)

Following suggestions from previous CAs meetings, the Commission presented a proposal for a survey for mapping the more stringent quality and safety requirements introduced by Member States, in addition to those laid down by the Directive 2004/23/EC and its implementing Directives. It was suggested to start with the mapping of the more stringent testing requirements, followed by additional surveys addressing issues such as donor selection and evaluation requirements and preparation processes requirements.

The first survey should be performed by sending to each Member State individualised questionnaires, pre-filled with the information on donor testing requirements provided for the 2013 implementation survey. It was agreed that the first questionnaire will also give Member States CAs the opportunity to propose additional topic(s) (besides donor selection criteria) for the next steps of the mapping exercise. The Commission expressed its intention to launch the more stringent testing requirements survey in July, with deadline in August or September, which may allow a presentation of its results during the next CAs meeting in December 2015. Once finalised, the replies from all Member States will be published on the Commission website.

2.5. Debrief from visit to FDA-CBER (COMM)

The Commission informed the group about a visit of representatives of the SoHO team in DG SANTE to the US Food and Drug Administration (FDA)/Center for Biologics Evaluation and Research (CBER) headquarters in Silver Springs. The meeting was attended by high level officials from several departments of CBER including the Office of Blood Research and Review (OBRR), Office of Biostatistics and Epidemiology (OBE), Office of Cellular, Tissue, and Gene Therapies (OCTGT) and Office of

Compliance and Biologics Quality (OCBQ). The meeting was an opportunity for both sides to present updates of their most recent regulatory work in the areas of blood (e.g. evaluation of novel transfusion products, MSM, reporting of SAR/rapid alert system, risk assessment) and tissues and cells (e.g. classification of tissues and cells and related products, authorisation of novel products and processes, authorisations and inspections of tissue establishments, vigilance system, import and export of tissues and cells).

The Commission pointed out some differences between the EU and US legislation in the area of tissues and cells and informed the group about several guidance documents elaborated by FDA/CBER and available for public consultation. Several Member States expressed interest to examine the regulatory changes envisaged by FDA. Two CAs (DK and IT) agreed to give a presentation during the next group meeting in December 2015, summarising the proposals put forward by FDA and examining their potential implications on the EU tissue and cell sector.

Overall Member States welcomes the possibility to increase mutual understanding between EU and US authorities and asked Commission to brief on further such exchanges.

2.6. Mapping of the US FDA vs EU requirements for tissues and cells (UK HTA)

UK-HTA representative informed that in preparation for the implementation of the Directive (EU) 2015/566 and taking into account that most of the UK imports come from US (i.e. approximately 25 000 units/year), HTA performed a comparison between the UK/HTA and US/FDA regulatory requirements in the area of tissues and cells. The mapping exercise had two main objectives: to identify the key regulatory differences between UK and US and to publish guidelines on the relevant legal requirements for both US suppliers and UK importing tissue establishments. The mapping exercise was performed together with the American Association of Tissue Banks (AATB) and FDA/CBER and covered topics such as: donor eligibility, preparation process validation, traceability documentation, adverse event/reaction reporting, processing environment. Several examples were given where similar requirements are understood and implemented in different ways, which may lead to delays/bans for using a certain tissue or cell in UK (e.g. in UK tests need to be performed on donor's serum or plasma, but a tissue imported from US may be tested using FDA kits approved using an alternative specimen) or increase the risks when a product is used in an EU recipient (e.g. for traceability purposes, donor data need be stored for 30 years in UK/EU versus 10 years in US).

The Commission welcomed this initiative and underlined the importance of this mapping exercise which could be helpful not only for UK, but also for other EU CAs and importing tissue establishments. Several MS expressed their appreciation and interest for the outcome of this exercise, pointing out that some of the issues require further research in order to reach consensus for their use (e.g. algorithm to be applied to assess the degree of haemodilution).

The group was informed that the outcome of this mapping exercise will be made publicly available on the HTA website, and that it can also be shared over CIRCA-BC.

2.7. Organisation of the oversight in the ART sector in Spain (ES)

The representative of the Spanish ART CA presented an overview of the oversight of their national ART sector. It was highlighted that the national healthcare system is decentralised, with the oversight tasks divided between the national and regional authorities (17 Autonomous Communities and two autonomous cities). While the national ART CAs is responsible for preparing guidelines and recommendations, for granting import and export authorisations and ensuring biovigilance, the regional ART CAs are in charge of authorising and inspecting ART TEs, organising and maintaining ART regional registries and guaranteeing the appropriate resources for the ART activities. The National Advisory Committee on ART has no regulatory tasks, providing only advice to the Spanish government in the area of ART (e.g. functional and structural criteria for ART TEs, dissemination of scientific information related to the ART sector).

The presentation also provided information on the number of ART establishments authorised at regional level and validated by the national ART CA, on ART activities and on the inspection system in this sector. The central authorities are preparing a register of ART establishments in ES, following verification of information obtained from regional authorities; At this point about 3/4 of all ART establishments are already in this central register, the remaining are subject to verification in the coming months. This registers will be basis for the inputs by ES into the Compendium of TE's (Eurocet128 exercise/coding platform).

The ES representative emphasised that a national action plan has been prepared, which includes verification of the authorisation and inspection of these remaining ART establishments, harmonisation of regional inspection procedures for the ART sector, update of legislation, and establishing and implementing an IT platform allowing a centralised management of regional ART repositories. This ART IT platform should collect information on the number of donors, ART TEs activity and ensure surveillance and traceability. Several strategic actions planned for the next period were mentioned, from guaranteeing the quality of the services provided (e.g. progressive increase of the use of vitrified oocytes), and reducing ART regional asymmetries, to streamlining the information flow.

In the subsequent discussions, several Member State underlined that due to the increasing cross-border distribution of reproductive cells, the authorisation of ART TEs according to the requirements of the EU legislation is essential for ensuring trust in the quality of products and services provided by an ART TE to patients in another Member State. In this respect, the group expressed interest for getting additional information on the inspections performed by the regional CAs (e.g. staffing, expertise of inspectors, outcome, number of non-compliance cases) and the current vigilance and traceability system at both regional and national level.

The participants and Commission expressed their appreciation of the presentation, and welcomed the planned work by the Spanish national authority. It was agreed that an update on progress should be presented during the next meeting (December 2015).

3. REPORTS

3.1. Update on the surveys on the implementation of the Tissues and Cells Directives and the implementation of the principle of voluntary and unpaid donation (VUD) for tissues and cells – main conclusions (COMM)

Following previous presentations in the December 2013, June and December 2014 meetings which provided preliminary results of the two implementation surveys (e.g. general implementation of the EU Directives and implementation of the principle of VUD), the Commission gave a full overview of its conclusions. It was emphasised that even though the surveys showed an overall adequate application of the current quality and safety requirements of the EU tissues and cells legislation in most of the responding EU Member States and EEA countries, they also revealed challenges in relation to the application and enforcement of the existing provisions as reported by various stakeholders (e.g. ambiguous, incomplete or lack of definitions of some key terms with various interpretations of these terms at national level, lack of requirements on the safety aspects regarding living donors, lack of generally accepted Good Tissue Practice/GTP endorsed by the EU legislation, lack of legal framework for risk-based inspections and joint inspections of tissue establishments, lack of EU-wide approaches to authorise tissue and cell preparation processes, etc.).

In the subsequent discussions, Member States supported these findings and called for common action to address the identified shortcomings.

It was clarified that the Commission envisages publishing the report summarising the main conclusions of the two surveys, accompanied by two staff working documents analysing and setting out in more detail Member States' replies. The Commission also explained the procedures to be undertaken for the publication of the report and staff working documents.

4. PRESENTATION OF PROJECTS, JOINT ACTIONS AND STUDIES UNDER THE HEALTH PROGRAMME

4.1. Update of the 2013 Joint Action (JA) on good practices on donation, collection, testing, processing, storage and distribution of gametes for assisted reproductive technologies and of haematopoietic stem cells for transplantation (Agence de la Biomedicine)

An update on the JA ARTHIQS (Assisted Reproductive Technologies and Haematopoietic stem cells Improvements for Quality and Safety throughout Europe) was given by a representative of the coordinator, the French Biomedicine Agency/ABM. The presentation included a brief outline of the main work-packages, with a focus on WP4/ART and WP5/HSC. As regards WP4, the group was updated on the status of the survey on mapping ART national systems and organisation of ART authorities in EU, for which the collection of data from the partners was finalised and the preparation of the report was on-going; after the publication of the report the survey should be fine-tuned and information should be collected also from the non-participating Member States.

Concerning WP5, after analysing the replies from the consortium partners to the questionnaire on the follow-up of HSC donors and taking into account their feedback, the revised questionnaire was circulated to all MS; analysis of the final results was planned

for June 2015, with a discussion of results and preparation of a common approach for the follow-up of HSC donors planned for September 2015. A summary of the answers to the questionnaire on the status of cord blood banking in the Member States was also presented; these data will be used as basis when defining the level of the technical requirements applicable to all cord blood banks, with a first draft expected for September 2015. For both WPs, the delays were explained and next steps were defined.

After thanking for the presentation, the Commission reiterated the importance of using the terminology in the EU legislation, of involving all Member States when collecting information for drafting guidelines/recommendations to be used at EU level and stressed the need to improve communication with MS, Commission and Chafea. Several Member States confirmed the need for giving extra attention to these points within this JA.

Some Member States felt that the questionnaire developed by WP4 was over-ambitious, and even though the ART sector is complex, should be more focused. Following a request from Member States not participating in the JA, it was agreed that CAs will have the opportunity to comment and provide feedback to the major deliverables/guidelines developed by the JA before their submission to Chafea.

The next update on the progress of the JA will be presented in December 2015.

4.2. Update from the study on the economic landscape of the tissues and cells sector (Rathenau Institute)

Several representatives of the consortium who was awarded the contract for the call for tender EAHC/2012/Health/19 made a presentation on the outcome/main findings of this study. The presentation reiterated the objectives of the study and focused on its key findings and conclusions. The main sections of the final report (horizontal, replacement tissues, haematopoietic stem cells, ART, looking forward) were presented and discussed individually, as there were numerous reactions from the floor.

After presenting the structure of the future report and the data sources some general observations were made, mainly on the status of tissue establishments, their cost awareness, price-setting mechanisms and application of VAT, import/export, and shortages. Some issues which may require further reflection were identified: the lack of cost-awareness in many public TEs, the existence of many small TEs working below the critical mass or the sub-optimal use of the stored tissues and cells. The need to increase awareness of costs and prices and a potential role for EU-level coordination of some of the activities in the tissue banking sector were raised.

The findings on cost and price awareness elicited numerous reactions, with several MS expressing concerns against the term "tissue and cell market" which may come in contradiction with the principle of VUD, and requesting a clear distinction between "price" and "cost", the latter being the term preferred. As regards some data on imports of tissues and cells into the Union, several MS questioned the presented findings, and requested amendments from the consortium.

The presentation on the haematopoietic progenitor cells (HPC) sector included data on the number of donors registered in registries and number of transplantations, an overview of cord blood banking in EU, as well as information on the cost structure in this area. The study revealed that many (bone marrow) registries have limited insight in the

breakdown of costs and their success depends on quality of HLA typing, speed of service and availability of donors. It was emphasized that HPC cannot become a commodity because the need for HLA matching prevents a traditional business model in this field. Increased interest in haploidentical transplantation (related "family" donors) might change the current landscape, becoming a threat for cord blood banks (short term) and registries (long term) and donor treatment in hospitals might increase substantially. The sector might be also influenced by the increased development and application of other therapies (e.g. with mesenchymal stem cells, dendritic cells, tumour infiltrating lymphocytes).

During the subsequent discussions, several Member States pointed out some inconsistencies and requested clarifications; it was specified that the probability of finding a donor depends not only on the size of a registry but also on how the system is organised at national level; the development of public cord blood banks might complement a national registry and decrease the dependency on external sources. The need for coordination between donor registries was also underlined, with a possible role to play at EU-level.

As regards the ART sector, the presentation focused on the data sources used, outlining the main ART hubs and Member States with large activities, and delineating the main trends. The difficulty in collecting reliable data in this particular domain was underlined, particularly on costs and pricing, where due to the large variability in treatment options and structures it was very difficult to compare between centres and Member States. Factors influencing the demand for ART treatments (e.g. ageing, rise of the non-traditional household, fertility preservation, scientific progress) were also analysed. The main differences across EU related to access to fertility care, reimbursement, donor anonymity and compensation system were also mentioned.

Like for the previous section, several Member States requested clarifications on data sources and terminology.

The last part of the presentation was dedicated to the future of the tissue and cell sector, the influence of new technologies, especially the impact triggered by related fields like advanced therapies.

In their final comments, even though the work of the consortium was appreciated, the group of the MS requested the inclusion in the report of a disclaimer stating that the Competent Authorities for Safety and Quality of Tissues and Cells, while consulted for this study, are not responsible for the economic and financial aspects of tissue establishments within their country.

The Commission clarified that the comments should be addressed in the final report, and that CAs will have the opportunity to provide corrections to the data regarding their country and comments to the report before its publication by Chafea.

4.3. Presentation of the results of the Eurobarometer survey for blood, tissues and cells (COMM)

The Commission presented the results of a survey aiming to assess the awareness and attitudes of EU citizens towards blood transfusion and tissue and cell transplantation. The study was based on the replies provided by citizens in all EU Member States to multiple

choice questions on whether they had donated tissues and cells in the past, their willingness to donate in the future, their motivation and readiness to accept a compensation, their perception on the safety of tissue and cell transplantation in their country and their support for the EU legislation in this field.

Overall, the study showed that over a third of respondents had donated a body substance in the past and two-thirds were prepared to donate at least one body substance during their lifetime in the future. Around half of respondents declared that they would donate tissues after death. As regards living donation (e.g. donation of bone marrow, cord blood), the survey revealed a higher than expected number of alleged donors, which may suggest a potential misunderstanding between the actual donation act and registration in a donor registry, or in case of umbilical cord blood between donation for public use and storage for family use. Similar results have been recorded for donation of sperm and eggs, therefore this part of the results have to be interpreted with caution.

Overall, cellular tissue transplantation was considered as safe by the majority of respondents and the main reason respondents gave for being motivated to donate was to help other people. In terms of compensation for living donation the three practices viewed as most acceptable were provision of refreshments, a free physical check-up and free testing. Around half of respondents were supportive of EU legislation and information to ensure the safety and quality of body substances. In contrast to blood donation, the fact that a significant percentage of the respondents didn't know how to answer to the questions regarding tissue and cell donation, may suggest that many EU citizens are not familiar with the topic of tissue and cell transplantation and the importance of donating not only blood and organs, but also other substances of human origin.

During the subsequent discussions, it was clarified that the survey was performed at the Commission request by a contractor specialised in designing surveys and performing face-to-face interviews, sampling the relevant and representative population and taking into account socio-economic and demographic data.

Some CAs recognised possible deviations in results from previous statistics/studies, and wondered whether over-reporting was partly due to lack of knowledge and partially to the wish of appearing in a favourable light in the eye of the interviewer.

The Commission concluded that the main message of the survey is that the willingness to donate is very high, therefore measures for improving the awareness on the importance of tissue and cell donation might help increasing the number of donors. The Commission will provide for a clarifying statement, pointing to possible points with difficult interpretation.

4.4. Presentation of the output of the 6th EUSTITE course for EU MS inspectors

On behalf of the organising team, the DK representative provided a brief overview of the 6th edition of the training course organised between October 2014 and March 2015 for EU MS inspectors of tissue establishments. It was underscored that the course was initiated and developed by the EU-funded project EUSTITE and promotes uniformity and consistency in the standards of inspection across EU. The current edition was structured in two parts, an E-learning phase of two months and a residential course hosted by the Blood and Tissue Bank in Barcelona which allowed for "hands-on" training. The training

course was highly appreciated by all the participants, being considered also highly useful for developing an EU inspection culture. The group was informed that due to the support of the University of Vienna (hosting the e-learning module), commitment from tutors and facilitators, and with a minimal funding a similar course will be proposed in 2016.

During the subsequent discussions, several MS expressed their support and appreciation for the course and confirmed their interest for its next edition. The Commission informed the group that the new JA on blood, tissues and cells will also address the issue of inspections' harmonisation, under which the contribution of the EUSTITE team to the planned training courses may be of interest. The idea of developing a similar training course for inspectors in the field of organs was also supported and could be discussed with the group of CAs for organ transplantation.

5. SURVEILLANCE AND VIGILANCE

5.1. Update on infectious disease risks

5.1.1. Epidemiological update (ECDC)

ECDC presented an epidemiological update focused on the evolution of the Ebola Virus Disease (EVD) outbreak in West Africa and the recent outbreak of MERS CoV in South Korea, for which the same safety measures as for SARS should apply. Information on a measles-outbreak in some EU Member States (DE, DK, NO, SE, UK) and other countries, mainly due to non-vaccination of children was also presented. Regarding the outbreak of ZIKA virus (ZIKV) in Brazil, the group was informed that the situation is escalating probably because of a possible co-infection with dengue. Because a treatment or vaccine are not yet available, prevention is based on personal protection measures similar to the ones against dengue and chikungunya. As regards the changing epidemiological situation of ZIKV in Brazil and the Pacific region, the EU SoHO authorities were advised to closely follow-up its evolution and if necessary, consider a temporary deferral of 28 days from donation of persons with a travel history to the affected areas (similar to the deferral period for West Nile fever). In areas endemic for Aedes moskito species, a preparedness plan to respond to future outbreaks of ZIKV infection should consider measures to sustain the supply of SoHO products.

As regards the ECDC' plans for 2016 activities on SoHO, three activities were mentioned: an expert consultation on the prevention of hepatitis E through SoHO, a study of prevalence of infectious diseases in blood and plasma donors and an assessment of risk of bacterial infections transmissible though SoHO. Concerning the latter, a meeting organised on the prioritisation of bacterial infections transmissible through SoHO is organised by ECDC on 24-25 September 2015 in Stockholm.

Both Commission and Member States representatives expressed their appreciation for ECDC's work.

5.1.2. Other – Member States will be asked whether they have additional information or updates to report

Member States were asked whether they have additional information or updates to report, but there was no report of any additional information on infectious diseases.

5.2. Update on the development of the EU tissue and cell coding platform (COMM)

The Commission presented an update on the status of the EU coding platform for tissues and cells, underlining that so far only 16 Member States nominated contact points for the platform and urged the others to provide them as soon as possible. The group was also informed that the Commission is revising the manuals for CAs and TEs developed by Eurocet128, and that further support should be available during the new JA on blood and tissues and cells, which includes a dedicated WP for supporting the implementation of SEC. Finally, the group was informed about the setup of the expert sub-group on the EU Coding Platform, which, in line with the requirements in Directive (EU) 2015/565 should support the Commission when updating the EU Tissue and Cell Product Compendium. The first meeting of the group was scheduled for the 4 July 2015, and the sub-group should report regularly to the Tissue and Cell CAs group.

5.2.1. Update on the preparation of agreements with product code providers

According to the requirements in Article 10c (3) of the Directive (EU) 2015/565, the Commission (DG SANTE) discussed and agreed with Eurocode and ICCBBA, the text of an agreement ensuring that updated product codes are regularly made available for the inclusion in the EU Tissue and Cell Product Compendium. It was clarified that the Commission envisages the publication of the Decision stablishing a model for agreements between the Commission and relevant organisations on the provision of product codes for use in the Single European Code in July 2015, followed by the signature of the two agreements in the next months.

5.3. Rapid alerts for tissues and cells/RATC (COMM)

The Commission presented the report of the second year following the launch of the new RATC platform in February 2013. The group was informed that compared to 2013, when 15 alerts were launched, 25 alerts were circulated in 2014. In the first 5 months of 2015 only 2 alerts have been recorded (more are expected during summer season when some outbreaks of communicable diseases are expected). The Commission informed the group that a new version of the SOP and of the User Manual was released in November 2014 and the 2014 RATC summary of activities should be available in the coming months. It was mentioned that discussions between the Commission and ECDC on exchanging alert information and on ECDC access to RATC are on-going.

5.4. Serious adverse reactions and events/SARE (COMM)

5.4.1. Results of the 2014 SARE annual reporting exercise (2013 data)

Following the presentation of the preliminary findings of the 2013 SARE exercise in December 2014, the Commission presented its final results. An overview of the figures for the total number of SAR and SAE, as well as a comparison of these data with the figures from previous years, were presented. The overview also included the usual breakdown of data per tissue and cell sector and type of SARE reported. Even though the overall reporting rate improved over the last couple of years, the Commission cautioned against drawing too positive conclusions based on these findings.

The group was informed that the summary of the 2013 SARE reporting exercise should be published by the end of summer, while the publication of the 2014 SARE Annual Report is foreseen for December 2015. Following a suggestion form the NL representative to develop the "Other categories" type of SAR, it was agreed that this issue

needs to be further addressed, if possible with support from the new JA on blood, tissues and cells which includes a vigilance work-package.

5.4.2. Launch of the 2015 SARE annual reporting exercise

The Commission informed that the 2015 SARE reporting exercise (for cases recorded between 1 January and 31 December 2014) should be launched by mid-June and the deadline envisaged is 31 July 2015. The group was informed that minor changes were operated only in the Common Approach document, and the reporting template will be identical with the one used in 2014. The group was reminded that following the agreement of Competent Authorities for tissues and cells and Competent Authorities for organs transplantation, vascularised composite tissues (e.g. face, arm) are considered to be covered by the Directive 2010/53/EC, therefore SAR following transplantation of such tissues should not be reported here. Several suggestions for the 2016 reporting exercise were introduced, such as changing the measurement units for some tissue and cells types (e.g. for skin from units to cm2, for the ART sector from units distributed to cycles), which require consensus from CAs. Upon a suggestion from the floor, it was clarified that an event causing the loss of multiple donations should be reported as SAE.

6. UPDATE ON THE REVISION OF THE EU MEDICAL DEVICES LEGISLATION (COMM)

The Commission updated the group on the latest version of the proposal for a new EU Regulation on medical devices, with a focus on the requirements related to the borderline between medical devices and the tissues and cells sectors. The new proposals from the LV presidency and other Member States were presented, highlighting the main points of concern (e.g. scope of MD is limited to derivatives extracted from non-viable tissues and cells as medical devices, a clear process to assess products combining medical devices and tissues and cells and to organise conformity assessments for such combination products (involving authorities from both sectors). Some follow-up during, and specifications after, further Council and EP negotiations will be important though.

General support was expressed for the current LV presidency proposal, which takes into account the concerns of the Tissue and Cell CAs. CA's were asked to continue liaising with their national counterparts in the medical devices sector and health attaches for providing timely feedback in case of further revisions of the proposed text. Commission and CA's agreed to continue passing information through the colleagues in this group (by email and in the next meeting).

7. VAT ON TISSUES AND CELLS (COMM)

The issue of VAT for tissues and cells was raised by not-for-profit operators following decisions in some Member States to include human tissues and cells among the goods to which VAT applies. In this respect, the group was reminded about the provisions in the EU VAT legislation (i.e. Council Directive 77/388/EC of 17 May 1977 amended by Council Directive 2006/112/EC) which explicitly exclude human organs, blood and milk, but not tissues and cells. Even though human tissues and cells are not mentioned, taking into account a wide interpretation of the term "organ", most of the Member States have been exempting them from VAT. It was explained that according to Commission services (i.e. DG TAXUD), products covered by the Directive 2004/23/EC (e.g. bone)

cannot be considered falling under the "organs" category, therefore are not subject to the tax exemption.

The group emphasised that, due to the principle of non-commercialisation which is strongly encouraged for the entire SoHO sector, tissues and cells for human clinical application should be also exempted from VAT. DG SANTE expressed support for this position and mentioned that this issue, which was already raised with DG TAXUD, needs to be further addressed.

8. AOB

8.1. Changing of procedures in a Danish sperm bank regarding blocking of non-partner sperm donors (DK)

The DK representative informed the group about two changes in national legislation regarding procedures related to sperm donors identified as carriers of a hereditary genetic disorder, effective from April 2015.

According to these current requirements, such donors are no longer placed in either quarantine or permanent block, but the sperm bank must update the donor profile/status on their website each time such information becomes available. Customers (clinics and private individuals) can purchase sperm straws from these donors only after having read and accepted a declaration (even without reading the donor information with the case description and risk assessment, with reference to Convention on Human Rights and Biomedicine). The sperm bank must also inform all customers that already purchased straws from such donors.

The group was informed that the DK CA plans to include restrictions in the national legislation coming into force in July 2015. The new requirements will prohibit the above mentioned procedure and reinforce the terms of quarantine and permanent block.

The CA also confirmed that, after reintroducing the "permanent block" status, it will continue informing CAs about such cases via the RATC platform.

8.2. "Three-persons-embryo" (COMM)

The group was informed about the approval in UK of the "three-persons-embryo" procedure, which refers to embryos created from three donors: one oocyte donor, one sperm donor and a mitochondrial donor. This technique is used to avoid serious mitochondrial diseases and has been approved albeit with a strict eligibility procedure.

Several members of the European Parliament expressed ethical concerns and suggested that the new UK legislation is breaching EU law. The UK HFEA was invited to prepare a presentation for meeting in December 2015 on the national practice regarding the three-persons-embryos.

8.3. Introduction of permanent deferral criteria for MSM (COMM)

The Commission briefly informed the group of the ruling in a case referred to the European Court of Justice (ECJ) concerning a permanent deferral from blood donation for men who have had, or have, sexual relations with other men (case C-528/13). According to the ECJ, such a deferral may constitute discrimination on the grounds of

sexual orientation and thus be a limitation on a fundamental right. Such a limitation could only be permitted if it could be justified as fulfilling an objective in the general interest, in this case, the objective of a high level of health protection for recipients. This limitation would also need to be proportionate i.e. it would need to be shown that the same objective could not be fulfilled through means less restrictive means such as effective testing or other less onerous methods. The case will now be referred back to the national court for a final ruling based on these criteria.

8.4. Other issues

NL suggested improving the communication between CAs between the regular, bi-annual meetings, by providing a "forum" function on one of the EU platforms. It was emphasised that even though RATC works very well it lacks this function, which for some topics may be extremely useful (e.g. sharing best practices, enquiring about interpretation of EU legislation). The Commission agreed to reflect on this suggestion and provide a response during the December meeting.