EUROPEAN COMMISSION
DIRECTORATE GENERAL FOR HEALTH AND FOOD SAFETY

Directorate B - Health systems, medical products and innovation
B4 – Medical products: quality, safety, innovation

Brussels, 2019

SANTE B4/IP ARES (2020)

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

Meeting of the Competent Authorities for Tissues and Cells 22 – 23 October 2019

Summary Minutes

The meeting of the tissues and cells competent authorities (CA) took place on 22 and 23 October 2019. The previous meeting had taken place on 13 and 14 May 2019.

PARTICIPATION:

- Competent authorities from all Member States (MS) participated in the meeting, with the exception of Bulgaria, Greece and Romania. The United Kingdom competent authority was not represented.
- All candidate countries except Albania, Montenegro, Republic of North Macedonia and Turkey attended the meeting.
- In addition, the representatives of the European Centre for Disease Prevention and Control (ECDC), the World Health Organisation (WHO) and the Council of Europe (EDQM) were present as observers. The Consumer, Health and Food Executive Agency (CHAFEA) representative could not attend the meeting.
- Private experts attended for specific agenda topics, as detailed below.

The representatives of the European Commission/DG SANTE unit B4 chaired the meeting.

1. WELCOME AND ADOPTION OF THE AGENDA

The chair welcomed the participants. Those representatives attending for the first time were asked to present themselves. The SoHO team members introduced themselves to the new representatives and they informed the meeting of the usual house rules.

2. ADOPTION OF THE AGENDA

The participants adopted the agenda without major modification.

DG SANTE invited the participants to declare any conflicts of interest. None were declared.

The Summary Minutes of the previous meeting had been approved by email and published on the DG SANTE website.

3. LEGAL MATTERS

3.1. Transposition and implementation of Tissues and Cells Directives (DG SANTE)

The Commission updated the group on the transposition of the EU tissues and cells legislation. The overall transposition check was finalised for all MS. There remains one on-going infringement proceeding which has been referred to the Court for failure to notify transposition of Directive 2012/39/EU.

3.2. Update on implementation of coding and import legislation (DG SANTE)

On the 2015 Directives on coding (Directive (EU) 2015/565) and import (Directive (EU) 2015/566), the Commission reported that all Member States had notified their transpositions. DG SANTE has been performing conformity checks.

3.3. Medical Device Regulation: interaction with TC competent authorities (DG GROW)

Following the discussion in the previous meeting, DG SANTE presented the topic and gave a short update on behalf of DG GROW.

4. EVALUATION OF THE EU BLOOD, TISSUE AND CELL LEGISLATION (DG SANTE)

DG SANTE summarised the results of the Blood, Tissues and Cells Evaluation (BTC Evaluation). The BTC evaluation was concluded on 11 October 2019 and the BTC report, the executive summary and related documents were published on the DG SANTE website: https://ec.europa.eu/health/blood_tissues_organs/policy/evaluation_en

DG SANTE invited the authorities to disseminate the report and the summary to national and regional authorities and the stakeholders active in the SoHO field.

The chair noted that the evaluation has highlighted the successes and shortcomings of the BTC legislation. The key findings emerging out from the evaluation were the following:

- Technical provisions of the legislation are out-of-date in a rapidly changing sector;
- Oversight provisions are not adequate to regulate today's BTC landscape;
- Some citizens groups are not adequately protected (donors, children born from medically assisted reproduction);
- Innovation in BTC is not optimally facilitated;
- Limited provisions to ensure BTC sufficiency.

The participants recognised and supported the findings. A number of participants referred to the need to revise the legislation. DG SANTE explained that to decide on the concrete steps, the Commission was to first consider the options for addressing the shortcomings.

DG SANTE informed the meeting that a conference to disseminate the evaluation findings and discuss them with stakeholders would take place on 28 October 2019. Over 200 participants had registered.

Note: video recordings of the conference are published on the DG SANTE website.[1]

[1] https://ec.europa.eu/health/blood_tissues_organs/events/ev_20191028_en

5. OVERSIGHT FUNCTIONS

Activities related to oversight functions, including the progress in the SoHO expert subgroups on vigilance, traceability and inspections were presented by different speakers.

The speakers highlighted considerable progress in the different subgroups. This work is recognised as very valuable to achieve a common level of knowledge/skills in national authorities.

5.1. INSPECTION

Update on the work of the Inspection Expert Sub-group (IES)

The IES 2019 Work Plan has been endorsed by the CASoHO Expert Group in May 2019 and the IES held its 2nd meeting on 20 June 2019. 20 participants from 14 MS participated in the meeting. A debrief on progress under the 2019 Work Plan was given. The IES work plan was to focus on guidance documents, coordination of training courses, oversight of joint/observed inspections, oversight of inspection system audits, dissemination of outputs. A document describing the work of the IES has been developed by the group and has been uploaded to CircaBC.

A participant asked if the output of the IES group could be incorporated in future changes to the legislation, e.g. joint inspections. The Commission mentioned that it would depend on a number of factors but that the output will be considered.

5.2. **AUTHORISATION (**GAPP WP5 and GAPP WP6)

This three-year EU funded Joint Action, GAPP, started in 2018 and aims to support the development of a common and optimal approach to both assess and authorise preparation processes in blood, tissues and cells establishments.[2]

GAPP WP5 is the core of the joint action and will propose an agreed approach to authorize establishments to develop and use innovative BTC. This will be a phased/step approach with temporary/conditional authorisations and requests from inputs from establishments and clinics. More clinical evidence will be required for new preparations that are more innovative. The day after this meeting, the NCAs continued discussing draft proposals from WP5. They presented NCA survey results, used as a basis for their work.

GAPP WP6 partners were preparing sets of quality requirements to assess BTC before release from blood or tissue establishments. One set focuses on blood, one n reproductive tissues and cells), one on non-reproductive tissues and cells.

Council of Europe (EDQM) noted that in the most recent edition of the Guide to the Safety and Quality of Tissues and Cells a series of new monographs have been added, defining critical quality criteria for specific tissues and cells. They suggested that GAPP should signal if there is a need for new monographs. The link between GAPP and EDQM experts should be strengthened.

[2] The Joint Action is led by Italy and the project consortium has 28 associated partners from 24 Member States and a large number of collaborating organisations.

5.3. TRACEABILITY

Update on the work of the Coding Expert Sub-group (CES)

The Coding Platform that supports the Single European Code for tissues and cells is in place since 2017. The Tissue Establishment compendium on the Coding platform includes information from 28 Member States and Norway and Iceland. There are over 4000[3] tissue establishments in the compendium, with the activities and authorisation status shown. 60 national and 29 regional authorities have been registered in the coding platform and are responsible for updating the information contained there.

To clarify implementation questions brought forward by the CAs on the implementation of the Single European Code, the Commission organised a dedicated meeting of the Coding Expert Sub-group on 15 May 2019. DG SANTE gave feedback from the coding expert subgroup meeting. The meeting focused on clarifying of the open issues and technical improvements and new features of the EU Coding platform.

DG SANTE considered a possibility of hosting the e-learning modules for the SEC developed by the VISTART joint action. The sub-group asked for volunteers to be rapporteurs to co-ordinate the group's work and to give updates at subsequent CA meetings. The group plans to conduct a survey of CAs on implementation of the coding provisions, exclusion and exceptions.

One authority highlighted a problem regarding the authorisation of import where distribution between MS is sometimes included as export/import.

More information on the SEC for tissues and cells is available at DG SANTE website.[4]

The next Coding Expert Subgroup meeting should take place in 2020 (date tbc).

Proposal for improving traceability of tissues and information to patients (ES)

Spain NCA has been working on a proposal to improve traceability of human tissues intended for transplantation and improved information for patients. A document developed and approved by the National Transplant Commission of the Inter-Regional Health Council had been shared via CircaBC prior to this meeting. The representative brought this proposal to the attention of the NCAs, as an issue to explore and develop in the near future.

COM thanked Spain for the initiative. It suggested passing this initiative to the Coding expert subgroup for discussion at meeting in 2020.

5.4. SURVEILLANCE AND VIGILANCE

5.4.1. Update on infectious disease risks

a) Epidemiological Risks - general update (ECDC)

The ECDC representative gave an epidemiological update informing the group of recent infectious disease transmissions that pose potential threats to safety of tissues and cells. The presentation which includes the relevant details has been published on the CircaBC platform.

b) Other - Member State updates

[3] April 2019

[4] https://ec.europa.eu/health/blood_tissues_organs/tissues/single_european_code_en

No Member State had specific national surveillance information to report.

5.3.2. Rapid alerts

DG SANTE provided the participants with a summary of alerts posted in the RAB and RATC platforms up to October 2019. A number of alerts (epidemiological alerts, Quality and Safety defects, information notices, bilateral enquiries and illegal/fraud cases) had been reported via the platform. The participants suggested that MS should use RATC more often to inform each other about outbreaks and if applicable, epidemiological alerts should be uploaded not only in RAB but also RATC. The Commission informed delegates that the 2019 RAB and RATC activities will be summarised in one single report for publication.

5.3.3. Serious Adverse Reaction and Events reporting exercise (EDQM)

The Council of Europe (EDQM) debriefed the participants on the final analysis of the 2018 SARE reporting exercise for Tissues and Cells. The numbers and types of SAR and SAE reported were presented, along with denominators, and the EDQM team highlighted areas where improvements could be made. The tissue and cell SARE draft report was shared by SANTE via CircaBC before the meeting. The presentation given at the meeting allowed the participants to address any questions and comments before the report was to be finalised.

The Commission thanked EDQM for the professional way they have carried out this work.

The Commission reminded all participants that the deadline of submitting the SARE country reports for 2019 had expired. However, a few countries missed the deadline. The Commission highlighted the need for Member States to submit their country reports on time.

The MS were invited to carefully consider the SARE Common Approach document and pay special attention to the changes in the reporting template. If there are two or more CAs in a MS, the representatives were asked to coordinate and send a single submission.

5.4.4. Update from the Vigilance Expert Sub-group

A sub-group to the expert group CASoHO E01718 working on vigilance across blood, tissues and cells and organs with the aim of improving the Commission's vigilance related activities, particularly the SARE and rapid alerts programmes.

An update of the work of the VES and the VES work plan was presented and necessary improvements in vigilance systems highlighted (SARE and RATC platforms).

It was reported that the VES would move on to work on Organs and RAB. An authority representative asked about a possible interaction with pharmacovigilance and medical device vigilance. The participants considered that it should be envisaged in the future.

A full VES meeting was scheduled for 19-20 November 2019 where a new wave of proposals for improvement will be discussed and prioritised for possible implementation in the future.

DG SANTE thanked the VES for their work and noted that this expert sub-group is providing a valuable link to the vigilance officers in Member States that are completing the SARE submissions each year.

5.5. CLINICAL OUTCOME DATA

5.5.1. Use of registries for clinical follow-up (ECCTR)

The ECCTR project, funded by the Public Health Programme, started in 2016. Within the project, eye banks, universities and professional associations from Italy, United Kingdom, Sweden, Netherlands and Ireland collaborate.

The objective was to build an EU web-based registry where ocular tissue transplant outcome data can be registered and shared. The project partners aimed to assess and verify the safety, quality and efficacy of human tissue transplantations in ophthalmic surgery and to build a common outcome assessment methodology for corneal transplantation.

In line with the objectives, a European quality registry has been set-up for corneal transplant surgery. It incorporates one of the largest web-based databases in the field. The online platform of the registry provides information on donor cornea origin, cornea recipient and surgical procedure facilitating evidence-based decisions in the future. This registry is maintained by the European Society of Cataract and Refractive Surgeons (ESCRS).

DG SANTE noted that this project fits into an identified priority area of work going forward and congratulated the partners for already having records from 12 countries. The final meeting of ECCTR took place in October 2019, just shortly after this CA meeting and the project was closed.

5.5.2. GAPP WP8 – Use of clinical date for preparation process authorisation

GAPP WP8 aims to introduce systematic methodologies for the evaluation of clinical data as part of the CAs' authorisation of processing activities. It builds a data model that will bring together data demonstrating interdependencies between preparation methods, preparation steps, test results and specifications of the final product, clinical outcome data demonstrating efficacy and safety of the product upon application to a patient. Preliminary views on how and which clinical data can be utilized by authorities to assess and (pre-) authorize (novel) BTC therapies were presented.

6. PRESENTATION OF ACTIONS UNDER THE PUBLIC HEALTH PROGRAMME

TRANSPOSE (TRANSfusion and transplantation: PrOtection and SElection of donors)

The project, led by Sanquin in the Netherlands, aimed to build risk-based guidelines and a standard Donor History Questionnaire for the procedures followed for collection of substances of human origin, including blood, plasma, gametes, haematopoietic stem cells and replacement tissues.

TRANSPOSE final results were presented and issues on donor protection echoed those highlighted in the BTC evaluation. The elements of TRANSPOSE might form a basis for possible donor protection measures, in the follow-up of the BTC evaluation exercise.

The CAs appreciated the work undertaken within the Transpose project.

Note: The project finished in early 2020.

7. INTERNATIONAL DEVELOPMENTS

7.1. Council of Europe (EDQM) update

EDQM presented their work on contributing to ensuring a high level of quality and safety standards in the tissues and cells field and harmonising the activities among European countries, facilitating uniform standards and practices. Specifically, EDQM focused on their recent activities in the BTC field summarising those of relevance to this meeting, including the Newsletter Transplant, the ongoing and planned projects in the field of tissues and cells including a preparatory study on trafficking of human tissues and cells, donor protection for tissue and cells donors, critical pathway for tissue donation and benchmarking physical examination practices of organ and tissue donors.

8.2. World Health Organisation

The WHO representative gave an overview about WHO programmes related to SoHO including transplantation of organs, tissues and cells, blood transfusion safety and blood and blood products. In particular, the representative shared insights on some therapy specific issues including faecal microbiota transplants, germline editing and breast milk banking.

9. Specific topics raised by Member States

Survey on sharing of surplus tissues (IT)

In the previous meeting, the Italian CA suggested exploring the possibility for a common exchange platform for surplus tissues and cells. Italy followed up on this with some questions to CAs to establish their interest in participating in such an exchange programme. SANTE thanked Italy for taking this initiative. A survey to gather answers to the questions was left open for additional few weeks. SANTE highlighted that this is work that needs to be driven by the authorities and experts. EDQM mentioned that their expert committee, CDPTS, runs a similar initiative for the sharing of frozen blood with rare blood groups and suggested sharing the information with the Italian authority.

Preparation of starting materials of human tissues and cells and extracorporeal chemotherapy products (FR)

The questions raised in the last Tissue and Cell CA meeting were followed up by the French competent authority representative in the meeting. The questions concerned the preparation of starting materials from human tissues and cells and the use of extracorporeal chemotherapy (classified as a cellular product compliant with the 6.2 article of the 2004/23 directive in France). The representative elaborated on the questions, explaining the issues. DG SANTE has shared the French questions via CircaBC prior to the meeting to facilitate the discussion.

To follow up on this, SANTE agreed to support France to launch a survey which could be useful also for the BTC Evaluation follow up. France was invited to prepare a draft survey which the Commission would launch on EU Survey.

Survey on oversight cord blood banking (NL)

The Dutch CA representative raised a question concerning commercial banking of cord blood, for autologous/family use. Cord blood banking is regulated, in most cases based solely on the EU tissue and cell directives. In the Netherlands, however, NetCord-FACT accreditation is an additional requirement for anyone handling cord blood. They are now are considering in which countries the same or a comparable additional requirement for accreditation (e.g. AABB accreditation) is included in the national legislation, specifically for private cord blood banks offering storage for autologous use. DG SANTE suggested that the Dutch CA shares with the full group the consolidated findings from their enquiries with other CAs when available.

10. ANY OTHER BUSINESS

DG SANTE gave a short presentation on new FDA guidance on fecal microbiota transplantation (FMT). EDQM noted that there is a chapter in tissue and cell guide on FMT.

The Croatian representative gave an overview of the Croatian Council presidency plans in the SoHO field during the presidency in the 1st half of 2020. The HR Presidency conference was planned on 16-17.03.2020 in Zagreb. *Note: due to Covid-19 pandemic the conference had to be cancelled.*

All participants were thanked for their active and constructive interventions during the meeting and were reminded that all presentations and associated documents would remain accessible in the CIRCABC platform.

The next Tissues and Cells Competent Authorities meeting is planned for 9-10 June 2020.

Note: due to Covid-19 pandemic the meeting was be replaced with a virtual one scheduled on 19 May 2020.