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

Joint Meeting of the Competent Authorities on: Blood and Blood Components Tissues and Cells Organs

6 March 2024, 09:00 - 13:00

BRUSSELS
Virtual event

Summary Minutes

PARTICIPATION

The meeting was attended by Competent Authorities from all 27 Member States, EEA countries (NO and IS) and candidate countries (BA and TR). Meeting was also attended by observers from the European Directorate for the Quality of Medicines (EDQM), the European Centre for Disease Prevention and Control (ECDC), the World Health Organization (WHO), the European Medicines Agency (EMA), the European Health and Digital Executive Agency (HaDEA), DG REFORM, DG SANTE Medical Devices unit, the Inspection Expert Subgroup (IES) and the Vigilance Expert Subgroup (VES).

1. Welcome, introductory remarks and adoption of the agenda

Participants were welcomed by DG SANTE, SoHO Team Leader (D2). Meeting attendees were informed on the agenda, including additional AOB points, namely on Santander Statement by ONT and HU Organs CA on HU PCY plan for a high-level conference on organs in Budapest. No conflict of interest was declared by any of the participants and no other points were requested to be added to the agenda. Updated version of agenda to be uploaded on CIRCABC, further presentations will be uploaded after the meeting.

2. Regulatory matters: Points for information / discussion

2.1 Introduction to the new SoHO regulation

SoHO team from DG SANTE presented a high-level summary of the key changes of the BTC legislation and overview of the overall timeline and process. The presentation focused on the changes to the Commission Proposal that were introduced during the negotiations with the European Parliament and the Council as most participants were already well-informed on the legislative proposal. A dedicated session for any specific questions from the B and T&C authorities is scheduled to be held on June 25 to clarify any doubts. Text is yet to be adopted, though a political agreement was reached on the 14th of December between the co-legislators, and the Council and Parliament are expected to adopt the text by this Summer. Currently, the text is undergoing legal-linguistic review and, subsequently, translation, so minor editorial and language changes might be made before a final version of the text will be adopted. The Text, as agreed politically in December, can be found in the substances of human area of the official European Commission website.

2.2 EU SoHO platform

Roadmap

In 2022, a feasibility study was conducted on preliminary requirements, specifications, and prototyping. Following this, a requirement analysis was performed to determine potential regulatory changes. Currently, the focus is on development actions, including design, data security, and a study on cloud architecture.

Expected functionalities

According to the updated legislative text, there will be an obligation to upload summaries of clinical studies to the compendium prior to their commencement. The platform will feature registries of entities and establishments, a compendium of SOHO preparations, SCB memberships, aspects of vigilance and alerts, supply flows, shortages, and supply alerts. Technical guidelines and details of MS Competent Authorities will also be included.

Design considerations and collaboration with CAs

Emphasis will be placed on cloud infrastructure and utilizing existing IT platforms, such as compendia from EU coding platforms. Protecting sensitive non-classified data (personal) is a priority, along with ensuring interoperability. A survey will be launched soon to gather information on national systems and interactions, including questions on reference data and vocabularies. Decisions regarding mapping and interoperability are still pending.

Comments from DG SANTE: Understanding existing MS systems is crucial for building upon them and ensuring interoperability, hence the importance of surveys. Authorities will be able

to automatically insert data from National Registries, with specifics on implementation yet to be determined.

3. Presentations on EU-funded actions

3.1 EU funded actions DG SANTE funded by EU4Health and 3.2 EU funded activities and implementation of the SoHO regulation

A summary was provided of the many current EU4Health actions ongoing or planned, many that will provide support for implementing the new Regulation, including an action to support implementation for new establishments that provide breast milk or FMT.

For CAs, two key actions are underway. Sight-SoHO, for training of CA personnel, has completed 11 e-modules and is organizing face-to-face workshops. Additionally, there will be a new action to provide support for the organisation of the supervisory functions under the new Regulation, with €4 million being allocated from the EU4H programme, intended for 2025-2027 use. However, this budget cannot be used to support all activities across all Member States, and focus therefore will be on initiatives that are supported by proactive national planning and commitment. Next steps involve initiating discussions with authorities to understand their needs and expectations and how the EU can offer support. DG REFORM in parallel is implementing the TSI program to provide technical assistance to Member States upon request, with applications accepted until October 31st, which can also provide valuable support to Member States that need to introduce reforms in preparation for the new Regulation (e.g., for blood and transplant services).

The ReaderShip project aims to assist hospitals in complying with the new legislation, focusing on efficient management and coordination elements, including efficient management of registration, ensuring traceability and vigilance, collecting activity data, and ensuring quality management of SoHO in the hospital.

A dedicated Joint Action GAPP-PRO will pilot the authorisation process for SOHO preparation authorisations, coordinating implementation across different Member States. Projects such as EuroTRaCTOR and EuMAR aim to simplify tasks for authorities and entities and collect data for annual activity reports.

The Commission will launch another action later this year that will promote coherence, especially regarding borderline products. Cooperation agreements with EDQM on technical guidelines are in place. Resilience of supply actions such as EGALITE and SUPPLY address supply-related issues in the SOHO sector post-COVID, focusing on accreditation programs, standards, and donor retention strategies.

Other actions, such as BRAVEST and SUPPORT-E, address crisis management, guidance, and good practices related to organs and convalescent plasma use.

4. Interactions Medical Devices-SoHO

4.1 DEHP-free blood bags

Blood bags containing di(2-ethylhexyl) phthalate (DEHP) as a plasticizer pose toxicity concerns in medical devices, including blood bags. The ban on the use of DEHP has implications for red blood cell quality however. It is necessary to, replace DEHP-containing blood bags without compromising red cell quality. The European Blood Alliance and BEST collaborative have separately developed guidelines for in vitro and in vivo assessments, respectively.

A Commission expert ad-hoc working group has been formed to devise a unified approach for the approval of validations on non-DEHP blood bags in the EU. This group aims to provide technical expertise, establish a forum for EU-level exchange, and create guidance documents to aid regulatory transition. The guidance documents will target CAs and applicants, offering recommendations for risk assessment and monitoring. Currently, the working group is reviewing existing guidance documents and literature while drafting the structure of the forthcoming guidance document.

4.2 Bone marrow collection kits

Following the withdrawal of companies supplying kits to the EU market two years ago due to the high cost of CE marking for low-volume devices, only one company has pursued CE certification under derogation. WMA highlighted in January that countries have implemented makeshift solutions, with one company being the sole one seeking CE certification. However, reliance on a single provider poses risks both from a safety and pricing standpoint. Medical Device colleagues stress that temporary solutions and derogations are not sustainable in the long term.

Most derogations for the supply of non-CE marked sets that have been granted to that company have expired and many are being renewed. The company has committed to obtaining CE marking for the bone marrow aspiration system within 24 months. It is suggested to explore extending national derogations to the EU through implementing acts. On a positive note, a second company, based in India, has applied for a derogation in one Member State with plans to apply for CE marking by January 2024, potentially alleviating supply issues. Authorities are encouraged to share any relevant information on supply challenges or resolutions. Additionally, a similar situation is anticipated for cord blood collection and processing kits, with orphan device designation being a possibility.

4.3 Nitrate contamination storage liquid

A storage liquid used for hematopoietic stem cells, has been found to be contaminated with nitrosamines in several batches. Authorities will receive further information on this in order to verify possible use within the HSC establishments in their territory.

4.4 In vitro diagnostics

The Commission presented an overview of a legislative proposal that is published and is the subject of a legislative negotiation. Intention of legislation to extend transitional period of in vitro diagnostic products, increasing availability and transparency.

Objective 1: Ensure availability of (high-risk) IVDs by extending transition periods, as transitional periods as initially foreseen would not be feasible for manufacturers.

- Proposal aims to extend transitional periods for in vitro diagnostic products.
- Focus on high-risk class D devices, including tests for blood and organ donations, and fast-spreading diseases.
- Approximately 200 ongoing applications and 600 expected, with an average conformity assessment duration of 18 months.
- Staggered and classified extension approach with conditions including continuous compliance and QMS implementation by May 26, 2025.

Objective 2: Preventing Shortages and Safeguarding Healthcare Systems

- When there is an interruption of supply of certain medical device the manufacturer anticipates interruption,

Objective 3: Enhancing transparency (EUDAMED).

5. Council of Europe EDQM Update

Activities relating to SoHO in the EDQM are supervised by the European Committee on Organ Transplantation and the European Committee on Blood Transfusion, which are responsible for establishing technical guidelines. The 22nd edition of the Blood Guide is expected to be published in March 2025 and will undergo consultation in May of this year. Contingency and emergency planning for blood supply will be included in the technical guidelines. Additionally, there is ongoing preparation for standardization and referencing to existing EU legislation in anticipation of the EU SOHO regulation. The revision process, including consultations, is being developed around the technical guidelines.

6. ECDC update

Updates on communicable disease threats in Week 9 include:

- Introduction of the Respiratory Virus Surveillance Summary (ERVISS) tool providing an overview of respiratory viruses in the EU.
- Surge in measles cases with 448 reported in January 2024, following a delay in reporting as over 1000 cases were reported in December 2023, resulting in one death.
- Global outbreaks of dengue and chikungunya, mainly concentrated in Latin America and Southeast Asia.
- Access to the ECDC SoHO page on the website under infectious disease topics, featuring specific disease surveillance pages.

Current ECDC activities:

- Virtual meeting of the Network Coordination Committee scheduled for March 19, 2024.
- In-person meeting of National Focal Points of the Organs Group to be held on June 18-19 in Stockholm.
- Progress on ECDC SoHO guidelines, with drafting relying on ECDC processes and scientific panels making decisions, submitted to SoHO-Net for liaison with national Competent Authorities.
- Completion of HIV panel meeting with commencement of HBV/HCV guidelines drafting. SoHO-Net to liaise with authorities for HIV Guideline Draft review from June to August 2024. Publication plan: HIV Guideline in Jan 2025, HBV/HCV at end of 2025, and end of 2026 for pallidum guidelines.

7. EMA update

Updates from the Biological WP include ongoing revisions to the position statement on Creutzfeldt-Jakob disease for plasma-derived and urine-derived medicinal products. Additionally, revisions to the FICX guideline and core SmPC for haemophilia are expected to be released in April. A new guideline on non-replacement therapies (anti-TFPIs) has been released and is currently under public consultation until April. Furthermore, guidelines for immunoglobulins are undergoing revision for subcutaneous and/or intramuscular administration, along with core SmPC, and new clinical investigation guidelines, with a targeted revision date around May. As part of the work plan, a workshop on drug development, regulation, and clinical practice in hemoglobinopathies, focusing on the diagnosis of sickle cell disease and thalassaemia, is scheduled for July 1st.

DG SANTE addressed the issue of supply actions/plasma supply shortages within the broader context of medicine shortages, emphasising specific needs for plasma-derived medicines. EMA highlighted that the updated position statement on CJD is likely to allow individuals who spent time in the UK between 1980 and 1996 to donate plasma for fractionation. The statement is close to finalization. Final endorsement from CHMP is expected by May for publication.

8. WHO update

The Blood Programme at WHO has developed the Global Database on Blood Safety (GDBS) to tackle policy inadequacies, insufficient blood supply, and limited availability of Plasma-Derived Medicinal Products. A series of guidelines have been created on global blood donation, testing, and processing policies, alongside workshops and webinars covering blood regulation, hemovigilance, and GMP for blood establishments. The implementation of the Action Framework is expected to enhance national systems' effectiveness and resilience in MSs, strengthening regulatory capacities at country and regional levels. The WHO Achilles Project, focused on safe plasma protein products and country support activities, is currently being implemented in Senegal and Indonesia, alongside a blood regulation self-assessment in Serbia. Upcoming deliverables include the implementation of patient blood management, costing blood establishments, GMP for blood establishments, and policy considerations regarding plasma exportation for PDMPs, along with guidance on donor selection.

In the Transplantation Programme, recent outputs include considerations on regulatory frameworks for human cells and tissues and ATMPS, with contributions from the EC and a report from the WHO Expert Committee on Biological Standardization. Collaboration with the Science Division is ongoing to address issues related to 3D bioprinting. Additionally, cooperation with the Spanish presidency of the Council on global convergence in transplantation, supported by the EDQM and the Council of Europe, has led to a successful summit covering So-HO-derived products. A new WHA, supported by EU MS and other countries, will review the WHO's mandate and address issues of access, availability, UHC, regulatory oversight, and trafficking.

9. IES / VES update

Inspection Expert Subgroup (IES)

Updates were provided on recent activities. A face-to-face meeting held in October aimed to address work clusters following a prolonged period of inactivity due to the COVID-19 pandemic, with a focus on developing a new work plan. One Work Package finalized Inspection Guidelines in February – Week 1, led by the Netherlands. Efforts are underway to integrate various aspects such as inspection report templates, detecting illegal fraudulent activities, and quality control laboratories into the inspection guidelines by the end of 2024. Additionally, coordination of training courses led by Italy in the SIGHT-SoHO action, joint inspections led by Austria, and oversight of the inspection system were discussed. The annual report, published in February, is available on the European Commission's website, and Member States are encouraged to nominate further representatives to join the IES.

Vigilance Expert Subgroup (VES)

Updates were provided on the work of the organ subgroup. A pilot EU level SARE data collection conducted in 2023 involved 15 Member States, followed by another survey with 21 Member States participating voluntarily. Discussions revolved around the potential repetition of data collection with improved tools and a prototype common approach.

Additionally, a second pilot testing draft guidance on the SARE submission exercise is scheduled for Q2. Progress on the revision of SOP within the rapid alert systems was discussed, aiming for harmonization across systems and encouraging sharing of encountered issues. Collaboration between VES and IES was highlighted, with Member States contributing to the Sight-SoHo project and participation in organs vigilance workshops. It was noted that VES membership has been strengthened, but there is still a need for members of the sub-group to accept leading roles in the work clusters. Finally, efforts to improve the usefulness of blood donor SAR data were discussed, including plans to reduce the number of submissions and increase data utility.

10. Any other Business

10.1 Santander Statement

The meeting documentation includes the Santander statement derived from a high-level meeting on the draft resolution of the WHA. This statement holds significant political value and is intended to influence both EU and non-EU MS. Efforts were made to translate recommendations into a draft resolution expected to be adopted by the WHA in 2024. Additionally, seven separate scientific papers are being submitted to the journal Transplantation. Once published, these papers will provide a high level of detail on various recommendations, which will be articulated in a manner that is very useful for CAs.

10.2 Upcoming meetings for CA

A conference on the new SoHO regulation is schedules for June 24, 2024 in Brussels. Invitations will follow. A face-to-face meeting with TC and B CA is scheduled for June 25 to discuss questions and answers on the SoHO Regulation. For blood, a face-to-face meeting of CA for blood and blood components is planned for November 12-13. Regarding organs, an informal meeting co-organized by the Hungarian CA will take place in Budapest on July 10, 2024. On September 24, a meeting co-organized by the Belgian CA is scheduled, and a high-level conference on organ donation and transplantation organized by Hungary is set for July 11.

11. Final Remarks

Attendants and speakers at the meeting were thanked for their participation and inputs. A particular appreciation was expressed to those Member States that held the Presidency of the Council during the negotiation of the SoHO Regulation and that worked intensively on improving the text.