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VISTART
VIGILANCE AND INSPECTION
FOR THE SAFETY OF TRANSFUSION ASSISTED
REPRODUCTION AND TRANSPLANTATION

"Vigilance and Inspection for the Safety of Transfusion, Assisted Reproduction and Transplantation" (VISTART)

NEWSLETTER – ISSUE 2
2018

Introduction to the Joint Action

VISTART is a Eu co-funded Joint Action (JA), meant to support EU Member States (MS) in developing and strengthening their capacity for monitoring and control in the field of blood, tissues and cells transplantation. The key objectives are to promote and to facilitate the harmonisation of inspection, authorisation and vigilance systems for blood, tissues and cells and to increase inter-MS collaboration and confidence in each other's inspection and vigilance programmes.

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Coordination (WP1 led by ISS - CNT/CNS Italy)

During this second year, the results reached and future steps of this JA were showed by the Coordinator and WP leaders during the meeting of the European Tissues and Cells Competent Authorities (CAs) meeting (February 21st-22nd, 2017) and Blood and Blood Components CAs meetings (December 1st-2nd, 2016 / June 22nd-23rd, 2017).

A very fruitful intermediate Plenary Meeting (MS.2) was held in Rome on April 11th-12th, 2017 in the presence of Associated Partners Collaborating Partners, External Advisory Board members, DG SANTE and CHAFEA representatives.

A speech on VISTART was held by the WP1 Scientific Responsible (Cristina Pintus) during the Session on the European Projects of the 26th Congress of the European Association of Tissue Banks (EATB - October 18th-20th 2107 Treviso, IT). Moreover a dedicated booth with dissemination materials was handled by CNT team (JA Layman brochure, 1st Newsletter, pens with JA logo and "The Inspection Guidelines for EU Competent Authorities Responsible for the Inspection and Authorisation of Blood and Tissue Establishments" – D.6 of WP6 charged on branded pen drives).

On the same occasion EATB Board, elected Angelo Ghirardini as postum honorary member of EATB. He sadly passed away in November 2016 without his experience on the Single European Code, VISTART WP10 would have not been able to perform this task as successfully it did. Angelo loved his job and worked with passion and precision. He will be missed by all as a professional and even more as a friend.

Communication and Public Awareness (WP2 led by HNBTS Hungary)

The Newsletter was completed by the WP2 with the help of the different WPs after the plenary meeting. The private part of the website (https://vistart-ja.eu) has been refreshed by the WP2 regularly (e.g. special the part of the event (13) and the collection of the basic or working documents). During the year the WPs presented their results on different national forum or congress. The statistic of the website can be seen on the private part of the website (Analised periode: 2016.April-2016. December and 2017.January – 2017. December).

Vigilance reporting for blood, tissues and cells (WP4 led by IPST Portugal)

WP4 aims to explore commonalities between vigilance in different areas, identifying opportunities for sharing of information and procedures to improve safety and quality across blood, tissues, cells and ART. The key objective is to harmonize work in the areas of annual SARE reporting, of Rapid Alert procedures (Group 1) and of horizon scanning for identifying new risks (Group 2).

For 2017 reporting period Group 1 worked on harmonizing the two existing EU documents on SARE annual reporting (one for blood and one for tissues and cells) and on unifying the existing EC Rapid Alert procedures for these two sectors – ensuring consistency and information sharing across the fields as required, acknowledging the specificities of the ART sector.

Deliverables linked to this work package for 2017 reporting period:
D4.1: Unified common approach on SARE reporting for annual reporting to EC – Month 20- june 2017
D4.2: Recommendations for harmonization of procedures and platforms for rapid alert for blood, tissues and cells and ART at the EU level – Month 20- june 2017

WP4 Meetings

3rd Technical Meeting of WP4, 10th March, 2017, Lisbon;
1st Meeting of the vigilance expert sub-group on improving SARE vigilance system 7th April, Brussels;
1st Plenary Meeting 11th and 12th April 2017, Rome;
4th Technical Meeting of WP4, Lisbon, 9th, June 2017.

Deliverables

All the comments and suggestions received following the Competent Authorities meeting held on the 1st December 2016 in Brussels have been added till 13th January 2017.
On 27th January the new versions of the documents have been send to SANTE;
After 1st Meeting of the vigilance expert sub-group on improving SARE vigilance system on 7th April, Brussels new versions of deliverables were produced and send to all participants;
After the 4th Technical Meeting of WP4, Lisbon, 9th, June 2017 the final version of the documents, with more improvements was send to the VISTART leader, Italy on the 21th September 2017:

- Harmonization and Improvements on SARE;
- Summary of proposed improvements on SARE;
- Rapid Alert procedures.

International collaboration for Vigilance Communication and new Preparation Process (WP5 led by ISS - CNT Italy)

WP5A aims to increase the participation of EU CA for blood, tissues and cells in the WHO Notify Project's vigilance didactic tool, the Notify Library of adverse occurrences in transplantation, transfusion and assisted reproduction (www.notifylibrary.org).
Three technical meetings have been held so far, whereas, a joint WHO Notify Project and VISTART JA meeting has been scheduled on the 1st and 2nd of March, 2018, in Brussels. As most recent dissemination activities, a presentation of the Notify Library with particular emphasis on VISTART WP5A has been delivered during the 26th Congress of the European Association of Tissue Banks (18-20 October, 2017, Treviso, Italy) and the 10th TRIP Biovigilance symposium (November 22nd, 2017, Rotterdam, Netherlands). Moreover, the VISTART JA has been cited in two manuscripts published by the international Notify partners (Whitaker B.I., et al. Hemovigilance and the Notify Library. Immunohematology 2017;33:159-164 // Strong DM. Tissue banking, biovigilance and the Notify Library. Cell Tissue Bank. 2017 Jun 30. doi: 10.1007/s10561-017-9639-0 [Epub ahead of print]).
The Vigilance expert sub-group (VES) has been established in January 2017with the objective to provide technical expertise to the Commission. As part of the next WP5A activities, the VES will be part of a network of vigilance to provide support and advice when an authority is dealing with a specific SARE (MS11). The WP5A will deliver the report of SARE investigation networking exercise by July 2018 (D5.2).

Other three WP5 part B meetings were held in Rome from October 2016 to February 2018 for a total of five technical meetings from the beginning of the project.
From the outcome of a survey about existing regulations in Member States on approval of new processing and on requirement for clinical follow up (FU) data on recipients and a review about clinical FU requirements in other sectors (Medicinal Products, Medical Devices, FDA, ESHRE), the established working group started to prepare "the Draft principles for Competent Authorities for the evaluation and approval of clinical follow up protocols for blood, tissues and cells prepared with newly developed and validated processing methodologies" (Deliverable 5.3). Its aim is to give the European Competent Authorities in the fields of blood, tissues and cells a first generic indication and the main principles on how to assess the quality and safety of innovative processing methods and on which kind of essential clinical information should become available in order to confirm the safety profile of the new therapy. In addition the group discussed about which clinical FU programs could be selected in order to monitor the outcome in patients treated with newly developed processing methods, focusing mainly on the correlation between kind of clinical FU plans degree of risk that remains unknown or unresolved after the validation procedures. The group has elaborated a table for linking four risk levels (negligible, low, intermediate and high) with four corresponding clinical follow up plans that differ according to scale, duration and complexity. In addition for situations where there is sufficient indication that the expected therapeutic value is high and can be life saving for severely ill patients, the Competent Authorities should consider a "conditional" Preparation Process Authorization. If there is a strong benefit-risk ratio for the recipients the clinical use could start even before the validation process has been completed. The draft version of the document is now ready and published on the private part of the JA website.

Inspection Guidelines (WP6 led by ANSM France)

The objective of the WP6, specifically the production of the Inspection Guidelines for EU competent authorities responsible for the inspection and authorization of blood and tissue establishments, has been successfully achieved, in conformity with the Grant Agreement. The Guidelines mainly aimed to establish a common framework for the conduction of inspections in both EU Member States and third Countries.
At the beginning of November 2016, the WP6 Leader asked to the European Commission to give some comments on the Guidelines before the consultation addressed to the national CAs, involving also the Leaders of WP7, WP8 and WP9.
On November 7th 2016, the consultation was officially launched. After the receipt of the comments of the EC and the closure of the consultation, the last WP6 meeting was organized on January 19 and

20, 2017 with the main objectives to discuss the responses to the consultation and the observations of the EC and, taking into account those responses, agreeing what final amendments ought to be made to the Guidelines.

The final version of the document was disseminated on April 28th, 2017 and it was used as the main reference document in the 2017 WP7 advanced training course.

Training of blood, tissues, cells inspectors with sharing of expertise across Member States (WP7 led by ISS - CNS Italy)

During the second year of the Joint Action, the activities of WP7 have been smoothly carried out achieving the results foreseen in the Grant Agreement.

Specifically, the second edition of the advanced training course on common approaches to inspection in the blood, tissues & cells, and ART sectors addressed to experienced inspectors have been organized as scheduled and delivered in two modules (e-learning and residential). The first announcement for information of the course was made in October, with a second one in December for registration. Both were addressed to the CAs for blood, T&C and ART of EU MS, including Serbia as candidate country.

In view of the training course, two meetings of the WP7 working group have been organised in Rome: one on January 23, 24 and 25, 2017 and the other on April 26 and 27, 2017 with the purposes of brainstorming and starting to set the materials for the course and of discussing and finalising the manuals (for both trainers and participants) for the face-to-face module, respectively.

The total number of the participants in the 2017 course edition was 35 representing 20 MSs.
The e-learning module started on the 24 of April and it ended on the 21 of May 2017.

After a "break the ice" week, the topics covered were the following:

- Independence and Impartiality/Managing conflict of interest, Recruitment, training and management of inspectors;
- Thematic inspections: SEC, import, process validation, desk-based inspection;
- The role of the inspector, Inspections of Third-Parties
- During the e-learning part, the trainers launched some topics/questions in order to stimulate the discussion and interaction among the attendees and the trainers.

The residential module of the course started on June 13, 2017 focusing on 7 topics structured in exercises, lectures and a role play:

1. Evaluation of Processes of Blood and Tissue Establishments;
2. Management of risks arising from the activities of an Inspectorate;
3. Import;
4. Procedures for identifying illegal and fraudulent activity (IFA);
5. Risk-based Approach: inspection activities, rapid decision-making procedure;
6. Classification of non-compliances;
7. Role Play on EU Joint Inspections.

On the last day, a final exam was distributed to the participants. A certificate of attendance was given to all the trainees and certificate of successful participation was given only to those who passed the exam with 60% of correct answers.

In 2018, a second edition of the course is foreseen to be delivered according to the Grant Agreement. It will be organized on the basis of the experience of the first edition and, most importantly, with some updates also with respect to the progress made in the other "Inspection WPs".

WP8 Establishment of a Framework for Joint Inspections (WP8 led by MOH RC Croatia)

During the second period, first back to back Tissues and Cells CA meeting was held in Brussels in February 2017 where WP8 leader presented to representatives of CAs objectives, deliverables, milestones and timeframe of the activities of the WP8.
Further, first technical meeting of WP8 partners was organised in Zagreb, Croatia in March 2017 where earlier prepared draft Code of practice was discussed and upgraded and first two joint inspections were scheduled.
In 2017 three Joint inspections were conducted. First inspection was performed in Croatia in blood establishment in May/June, second was organised in Austria in multi-tissue establishment in October and third was in Bulgaria in ART establishment in November 2017. After each inspection a report on performance was written. Reports were shared among WP8 partners but also with WP6, WP7 and WP9 partners.
All performed joint inspections were graded by the partners as very successful and valuable experience. Lessons learned in inspections were used to amend and advance the deliverable-Code of practice. By the end of a project two more inspections will be conducted after which Code of practice will be finalised.

A Voluntary Programme of Inter-Member State Inspection Systems Auditing (WP9 led by HPRA Ireland)

WP 9 is led by the Health Products Regulatory Authority (HPRA) in Ireland. This WP has the long-term aim of supporting MS in verifying the equivalence of each other's blood, tissue and cell inspection systems. WP9 started at M12 (September 2016) and the WP leader, HPRA held the 1st working group meeting on February 1st – 2nd 2017 in Dublin.

One document "The CESIP Manual" has been drafted consisting of information on the auditing programme with procedures and checklists provided for in appendices that can be used, as required, by the auditors and auditees.
The documents were further refined via email following the meeting and working drafts were finalised after the 2nd WG meeting on 30th - 31st March 2017 in Dublin.

3 pilot audits are foreseen within the WP. The first pilot audit was carried out in Latvia in August 2017. The two further pilot audits will be performed in 2018. The CESIP Manual will be subject to review and update in accordance with the outcomes and key learnings from the pilot audits performed in 2017 and 2018 as part of this WP.

The WP also calls for the definition of an auditor training programme, production of teaching material for attendees and the performing of CESIP auditor training. An overview of CESIP auditor training programme has been defined. The experience from the pilot audits will be used in the development of the training material and it is foreseen to perform CESIP auditor training in 2018 after the completion of the pilot audits and finalisation of The CESIP Manual.

A 3rd WG meeting was held on 30th November -1st December 2017 to discuss the outcome of the first pilot audit and to discuss the training programme. Project timelines for 2018 were discussed and agreed
The sustainability of the project was also discussed at this meeting with a view to preparing a proposal in collaboration with the other inspection related work packages (WP6, WP7 and WP8). A meeting between the work package leaders to discuss proposals for sustainability was held on 1st February 2018.

A promotional leaflet, providing CA's / Inspectorates with information related to the CESIP Audit Programme and highlighting the benefits of participation was disseminated to all MS CA/Inspectorates in the field of blood, tissues and cells (including ART).

CAs / Inspectorates who wish to participate in the CESIP Audit Programme as an auditee and who also wish to nominate a candidate of suitable inspector experience to attend the Audit Training Programme are invited to provide an expression of interest by contacting the CESIP Audit Programme at the following email; cesipmail@hpra.ie.

Implementation of the Single European Coding System in Tissue establishments (WP10 led by ISS - CNT Italy)

Supporting the implementation of the Single European Code and providing guidance to EU Tissue and Cells Competent Authorities and to TEs across the Union has been WP10's mission ever since VISTART started, in 2015. It goes without saying, that the best way to provide this kind of support is to establish a direct contact with those in need for support and therefore, the WP10 team joined the main scientific congresses in order to meet with professionals and users.

In Hannover, Germany the staff participated in the 25th Congress of the European Association of Tissue Banks, EATB from November 23rd to November 25th, 2016 where a roundtable on "IT European Single Code for Tissue Workshop: Upcoming implementation Single European Code: set-up, next step/timeline, and concrete to do's for EU tissue establishments" was held.

In Marseille, France professionals could reach the WP10 team at the 43rd Annual Meeting of the European Society for Blood and Marrow Transplantation, EBMT from March 26th to March 28th, 2017. Following the online learning course on the Single European Code, hosted on CNT Platform from September 5th to October 17th, 2016; the leader of the Evaluation WP2 submitted a survey to participants to collect comments and opinions on the impact of the course. The response rate to the questionnaire was 44% (27 respondents out of 62 who received it). 67% of the 20 users who completed the course, agreed that the objectives were clearly explained and 61% agreed that the course was well organized and easy to follow.

WP10's achievements were presented at the Interim Plenary Meeting in Rome, from April 11th, 2017 to April 12th, 2017.

In November 2017, upon invitation from the editor, the scientific journal Transfusion Medicine and Hemotherapy published an article by WP10's team, titled "From the EU Legislation to the Application of the Single European Code: Support to the Implementation" on its "Coding of Tissue and Cell Products" issue. The article represents WP10's additional effort to reach the widest public possible and provide important information on the SEC in the clearest way.

Coordination with other projects or activities at European, National and International level

Implementation of Single European Code (SEC): the VISTART WP10 offered a number of opportunities to EU T&C TEs and to all the Professionals across EU working in the provision of T&C at human purpose to comply the new EU Directive on SEC to give them an overview of the legal background and the tools that have been developed Implement the legal requirements on SEC in their country.

Notify Library: Taking advantage of the role of CNT as Collaborating Centre of WHO managing the Notify Library (www.notifylibrary.org), VISTART WP5 partA is working to increase the involvement of EU MS CAs in the WHO's Notify Library initiative, where adverse events and reactions of didactic value are evaluated to share the lessons learned as widely as possible, in support of improved safety and quality.

Euro-GTP II: Euro—GIP II (http://goodtissuepractices.eu/ where CNT is leader of WP5) will determine how TEs and end users must proceed to gather information about safety and efficacy of novel processing methods. On the other hand VISTART (WP5 partB) is working on what is to be assessed by the CAs in order to authorise new T&C&B products, processes and therapies/indications. It will elaborate regulatory principles for CAs for the evaluation and approval of clinical follow up protocols (basic elements) for T&C&B prepared with newly developed and validated processing methodologies, instead Euro—GTP II will propose a tool to identify the risks of new preparation processes and to plan clinical follow up plans proportionate to the degree of risks identified with the tool.

The European Cornea and Cell Transplantation Registry (ECCTR - http://www.ecctr.org/) is a European Consortium that aims to build a common assessment methodology and to establish a EU web-based registry and network for academics, health professionals and authorities to assess and verify the safety, quality and efficacy of (new) human tissue transplantations in ophthalmic surgery. The WP5 partB group could appreciate how the ECCTR registry is successful in gathering results about the follow up period. The proposed collaboration between ECCTR and WP5 part B will combine the experience of the clinical registry and the definition of regulatory principles of VISTART on clinical follow up of tissue transplants.

Moreover, this JA will take full advantages of the work and results of previous EU funded projects in the same fields namely: SOHOV&S, CATIE, EuBIS, EUSTITE, EUROCET128, ARTHIQS.

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