Newsletter 4

(April 2022 - Final Layman Report)

FacilitatinG the Authorisation of Preparation Process for blood, tissues and cells

GRANT AGREEMENT NUMBER - 785269
May 2018-January 2022

Co-funded by
the Health Programme
of the European Union

Introduction

Since the directives 2002/98/EC, 2004/23/EC, 2005/61/EC, 2006/86/EC were adopted in Europe, significant technical developments have taken place and the complexity of preparation processes of blood, tissues and cells, has greatly increased.

A variety of process steps has been modified or introduced into routine use and new resulting products are being used in the patients.

Increasing complexity of processing can bring significant quality and functionality improvements of the products for patients' treatment, and/or more efficient use of donations, but it may also bring increased risk, particularly as the level of complexity brings the final product towards the borderline with medicinal products.

The assessment and control of risks should be ensured via the preparation process authorisation procedures in place in each Member State.

GAPP Joint Action was an ongoing 45 month EU project which addresses the authorisation of preparation processes in blood and tissues and cells aiming at:

01 Increasing consistency and efficacy of Competent Authority (CA) regulatory activities through harmonisation of EU-level tools for authorisation procedures for preparation processes at Blood and Tissues Establishments,

02 Developing a concept model for a European knowledge-sharing platform that can support CAs in the assessment and evaluation of novel preparation processes of products, and

03 Establishing an international network of specifically trained assessors / inspectors that can support CAs in the assessment and evaluation of preparation processes of products.

During this final period of the GAPP JA, the Covid19 pandemic unfolded during the course of the Action, which also led to its subsequent extension until end of January 2022. In spite of the consequent (social and travel) restrictions imposed, which acted as a constraining factor not allowing partners to fully implement dissemination-communication and training face-to-face activities, a number of events took place remotely and important work has been done by the Action's participants towards the achievement of the GAPP JA goals.

Final Layman Report

In this Final layman report , we are happy to share the final outcomes of the GAPP Action. Due to the impact of COVID-19 pandemic the original timeline of the Action was extended till January 2022.

Different deliverables and reports have been produced or drafted which will be discussed in this issue. All participants had a very positive experience in the jointly conception of GAPP's deliverables. So far, GAPP has reached a wide audience through electronic material, the webpage but also the social media, registering high engagement rates on Facebook and Twitter.

This brochure is part of the joint action '785269/GAPP' which has received funding from the European Union's Health Programme (2014-2020)

GAPP Training

In the framework of WP 10, the GAPP JA has organized the 2021 *Advanced training course on common approaches to preparation process authorisation (PPA) in the blood, tissues & cells, and MAR sectors.* The GAPP training course was composed of three parts: the e-learning module, 1 week live session and 1 week forum with final examination. Successful participants received n. 4 ECTS (European Credit Transfer and Accumulation System).

OBJECTIVES: The main objective of the Action was to facilitate the development of a common and optimal approach to assess and authorise preparation processes in blood and tissues establishments giving particular attention to innovative processes under development. Therefore, GAPP aimed to ensure that blood and tissue and cell products and related processes are subject to European safety and quality requirements considering that, at present, there is not a full harmonisation among the Member States.

Based on the recognition of the common principles of quality and safety of blood and blood components, tissues and cells, the harmonisation of some of the guidance and training tools at the European level should be considered as a strategic step to ensure a high level of the protection for patients and donors.

TARGET AUDIENCE AND TRAINING MATERIALS: The training course was delivered remotely and co-organized by the WP10 leaders (the Polish Krajowe Centrum Bankowania Tkanek I Komorek) in cooperation with the Italian National Blood and Transplant experts. The audience was made of experienced inspectors/assessors for blood establishments (BEs) and tissue establishments (TEs) processing reproductive cells for medically assisted reproduction (MAR) and non-reproductive tissues and cells.
The main reference document will be the "Overall Guidance on organization of PPA system" and the following technical annexes:

- Annex I – authorisation of changes in donation, procurement and collection, processing, preservation, storage and distribution;
- Annex II – assessing the quality and safety for donor/donation testing, pathogen reduction and sterilisation steps as part of PPA process;
- Annex III assessing clinical data as part of PPA;

GAPP Training

In addition, a concept of a knowledge sharing platform on PPA between European Union CAs was also presented. The platform allows for a standardised, electronically supported assessment of quality, safety and efficacy of blood, cells and tissues, in the case of state-of-the-art as well as innovative processing procedures

OUTCOME OF THE TRAINING. Participants have:

- gained the skill to perform risk assessment for the novel BTC and changes in their preparation processes, using the EuroGTP II risk assessment methodologies;
- learnt how to define the extent of the required information for PPA based on the level of risk related to the novel BTC or change in the preparation process;
- known what to take into account when assessing the aspects affecting the microbiological quality and safety of blood, tissues and cells (BTC), including:
    - competence of laboratories performing donor/donation infectious disease testing and microbiological testing of BTC,
    - reliability of the donor/donation infectious disease marker test kits,
    - effectiveness of pathogen reduction during BTC processing,
    - effectiveness of sterilisation methods during BTC processing,
    - microbiological status of final BTC products;
- known how to evaluate the clinical component of the Preparation Process Dossier (PPD); get to know the WP9 platform supporting the application for PPA and assessment of PPA dossiers;

So far, nearly **forty experts** from the EU MS CAs have been successfully trained by the Action. The aim is to train as many as CAs inspectors/assessors as possible, and therewith develop an international network of experts that can support CAs when evaluating new preparation process authorization.

A consolidated manual for training is now available

This brochure is part of the joint action '785269/GAPP' which has received funding from the European Union's Health Programme (2014-2020)

Guide on organization of PPA system

The guideline defines novelty and significant change. A significant change will have been identified through initial identification as a novelty and the subsequent risk assessment process described in EuroGTP II. The guideline discusses the steps in relation to the PPA and is divided into four sections: application process; technical annexes; review and evaluation; framework for CA. The guideline proposes the types of authorisation to be granted based on the information supplied by the applicant and the benefit risk ratio demonstrated. The proposed authorisations, are full authorisation, conditional authorisation and a refusal of authorisation. The guideline also includes a PPD template to enable CAs to create their own guidelines for specific PPDs, and a template to aid CAs in the review and assessment of PPDs.

Three technical annexes were developed by WPs 6, 7 and 8 to facilitate the development of a common approach to assess and authorise preparation processes in blood tissues and cells establishments (BE/TE) to be referenced in conjunction with the guideline.

TECHNICAL ANNEX I on authorisation changes in donation, procurement and collection, processing, preservation, storage and distribution addresses the methods and criteria to be used in the authorisation of novel preparation processes (PP), or changes to existing PP in the four fields of Blood, Tissues and Cells, Haematopoietic Stem Cell Therapy and Medically Assisted Reproduction. The quality and safety of Blood, Tissues & Cells intended for human application has a critical impact on patients. PPA are, with the exception of MAR where the intention is to facilitate the creation of a human life, conditioned by the quality and safety of the final products they prepare.

The evaluation of a preparation process will be based on the appraisal of its critical processing parameters (CPPs) and, where applicable, on the identified critical quality attributes (CQAs) of the products it prepares, again with the exception of MAR where it is nearly impossible to define the quality of reproductive tissues and cells and where Key Process Indicators (KPIs) are proposed instead. These recommendations provide guidance on how to ensure these CQAs (KPIs) and CPPs are met through in vitro studies, process validation and clinical investigation and clinical follow up.

Guide on organization of PPA system

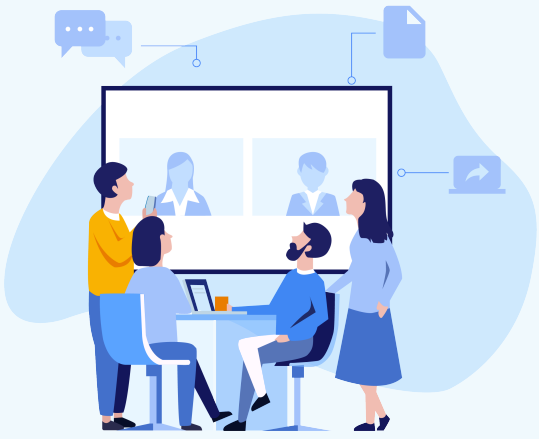
TECHNICAL ANNEX II on assessing the quality and safety of donor testing, microbial inactivation and sterilisation steps as part of PPA describes aspects which the Competent Authorities (CA) of Member States (MS) should take into account when assessing:

- competence of laboratories performing donor/donation infectious disease testing and microbiological testing of BTC
- reliability of the donor/donation infectious disease marker test kits
- effectiveness of pathogen reduction during BTC processing
- effectiveness of sterilisation methods during BTC processing
- microbiological status of final BTC products

Microbiological safety will be assessed in relation to the potential presence of bacteria, viruses, fungi, parasites and prions in BTC (as defined by GAPP).

TECHNICAL ANNEX III on assessing clinical data as part of Preparation Process Authorisation (PPA) provides Competent Autorities with key principles as to:

- which factors should be considered by CAs when assessing the clinical component of a Preparation Process Dossier (PPD) for completeness and suitability;
- when a Clinical Follow-up Plan (CFUpP) or a Clinical Investigation Plan (CIP) should be requested in order to support the authorisation of a new BTC preparation process and/or therapeutic application;
- what elements should be included in the CFUpP or CIP;
- what type of clinical data would be required to determine the safety and efficacy of human BTC applications for therapeutic use in recipients.



This brochure is part of the joint action '785269/GAPP' which has received funding from the European Union's Health Programme (2014-2020)

Knowledge Sharing Platform & Risk assessment

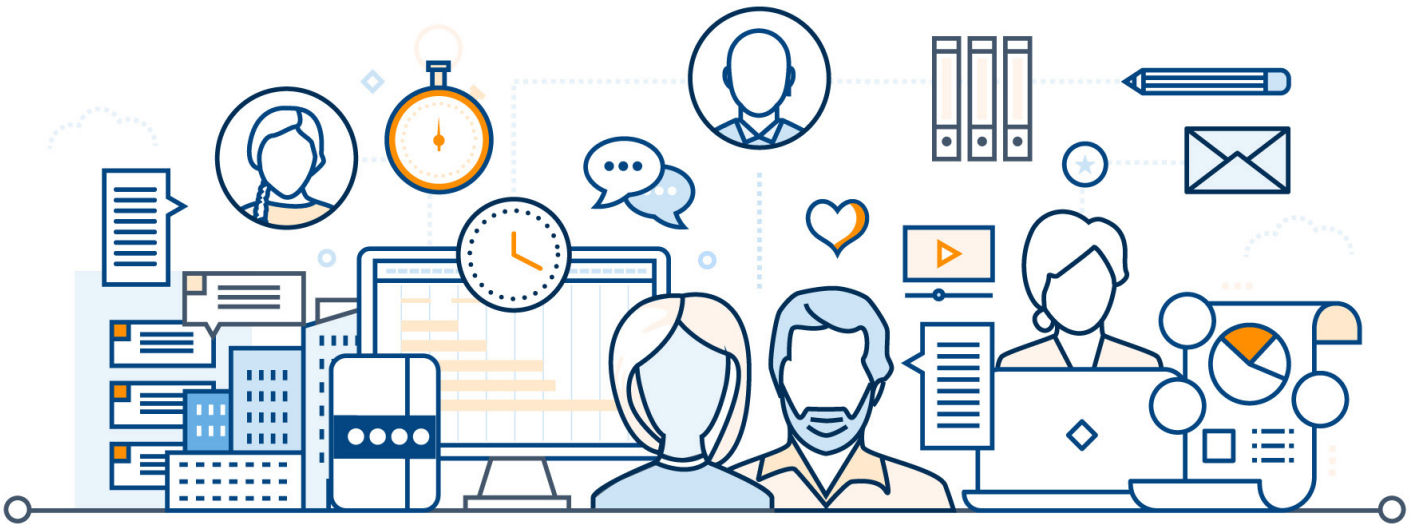
KNOWLEDGE SHARING PLATFORM The concept was developed considering the results of other work packages of the GAPP Joint Action and discussions with the consortium experts. The EDQM Guides and EU directives as well as previous EU projects were taken into account.

In the first step, the data from WP6, WP7, and WP8 were integrated in a single framework (see Deliverable 9.17). In the second step, the framework was expanded into a framework for electronically supported PPA. Finally, an operational concept for a platform for PPA of BTC was created based on these two deliverables. A demonstrator as a proof of concept, was programmed and is provided as a Docker container image. The concept and demonstrator can be used in a future project to create a fully functioning platform for PPA of BTC in the EU.

EUROGTP II Interactive Assessment Tool – Blood. The blood component specific chapter was developed in the framework of GAPP Action in order to provide recommendations and to improve the quality of healthcare delivery within the field blood components and to answer to the mandate of the GAPP Action to adapt the outcome of previous projects to the blood sector.

The Euro GTP II Methodologies (Annex I – Methodologies Wall Chart) and Interactive Assessment Tool (https://bloodtool.goodtissuepractices.site/) has been developed to assist professionals involved in the provision of BC to:

- Determine if a BC or preparation process has any novelty (Step 1)
- Assess the risks associated with the BC or preparation process (Step 2)
- Determine the extent of any studies and/or follow up required to assure the safety and
- efficacy of BC. (Step 3)



GAPP faces

Massimo Cardillo

Vincenzo De Angelis

GAPP JA deliverables should be considered as an important milestone that improves preparation practices, and eventual outcome for BTC recipients across Europe. The Action introduces the use of clinical data within the authorization procedures

The GAPP Action also identifies the need for up-to-date guidelines based on the evolution of research, therapeutics and information technology, while it lays down the foundations of a central knowledge sharing platform at an EU level which can be updated, easily accessible and transparent

> “The objectives of the Action is to facilitate the development of a common and optimal approach to assess and authorise preparation processes of Blood, Tissues and Cells harmonizing the authorisaion procedures and assuring the safety and effectiveness”

Stefaan van der Spiegel

The GAPP Joint Action has provided a stepping stone for the upcoming revision of the legislation on Blood, Tissues and Cells, which the European Commission plans to adopt in the coming months.
This work brings greater assurance when receiving safe and effective treatments. The result is more harmonized healthcare for patients and donors across the EU, with standardized procedures and processing protocols, that will be better aligned with the rapid, high-level and dynamic scientific and technological development of the field.
The new EU framework will bring better and more up-to-date safety and quality standards, facilitate innovation and allow for better access to BTC therapies. The new common framework will allow for more smooth cross-border exchanges of BTC, and the availability of services and novel products or treatments to EU citizens. The initiative extends also strengthens donor protection and donor care.

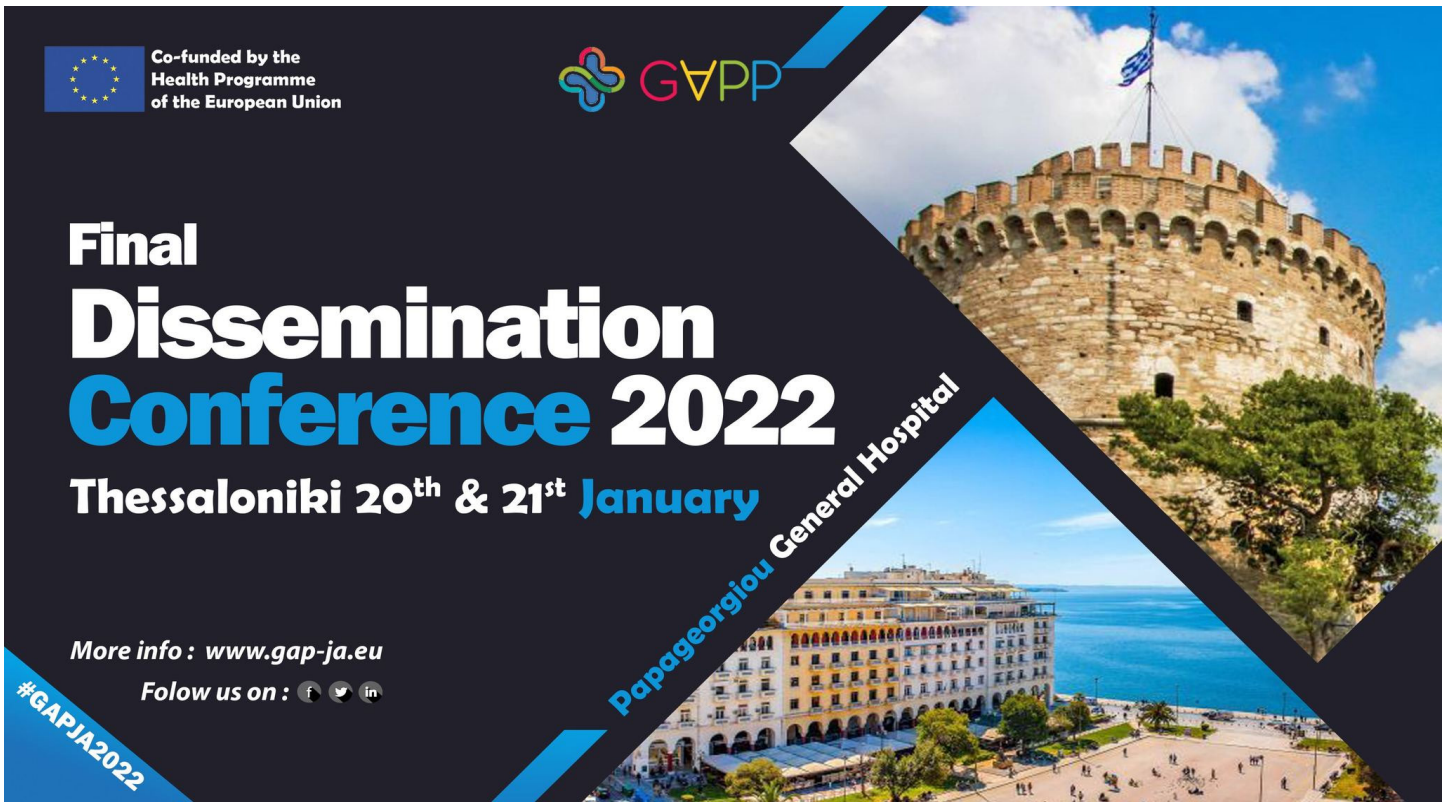
This brochure is part of the joint action '785269/GAPP' which has received funding from the European Union's Health Programme (2014-2020)

Final Dissemination Conference

GAPP JA Final Dissemination Conference

The **Action's Final Dissemination Conference** (D2.5, MS8, MS7, MS10) was developed and implemented in-house, with extensive and constructive meetings and communication between GAPP JA collaborating/ associated partners, WP leaders and the European Commission DG SANTE officers. The Final Dissemination Conference was held as a **hybrid event** in **January 20th & 21st, 2022** with the host location being **Thessaloniki, Greece.**

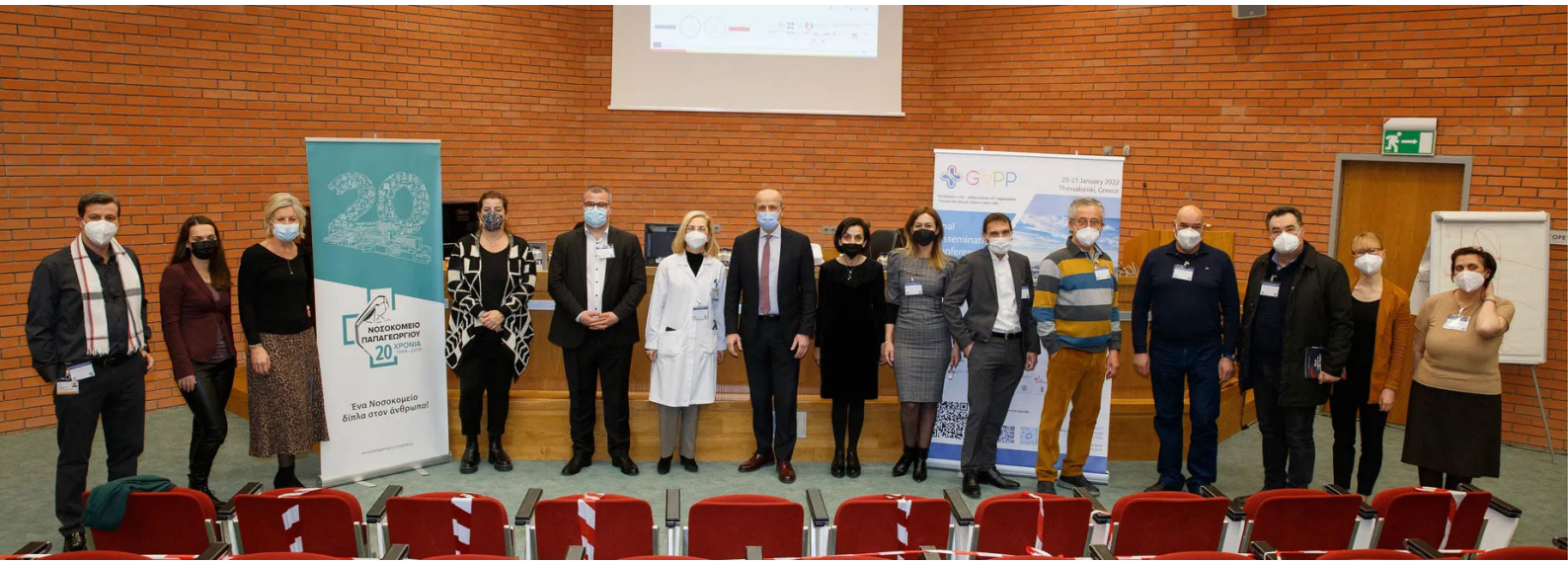
The GAPP JA Final Dissemination Conference successfully brought together a diverse audience and key high-level representatives from EU Institutions, and partners, scientific associations as well as donors and patients' associations to stimulate multi-stakeholder dialogue and views, and promote optimal use of SoHOs and a uniform approach across the EU.



Final Dissemination Conference

Day one of the event comprised of the **presentations of WP leaders** along with an overview on the work carried out in each WP during the course of the Action.

Day two, was dedicated to interactive sessions and discussions on **how to effectively bridge the gap between science and effective policies**, taking a closer look at governance, the current state-of-play in the EU and beyond, including legislation requirements and standards for accreditation along with the role of Associations and Registries. Discussions looked at and the next steps towards BTC policy implementation and the impact of the revision of the BTC legislation on patient and donor safety, and the quality of treatments. A special effort was made to attract a diverse audience and to set up panel speakers to contribute with their expertise to fruitful discussions on trending issues debated across the EU.



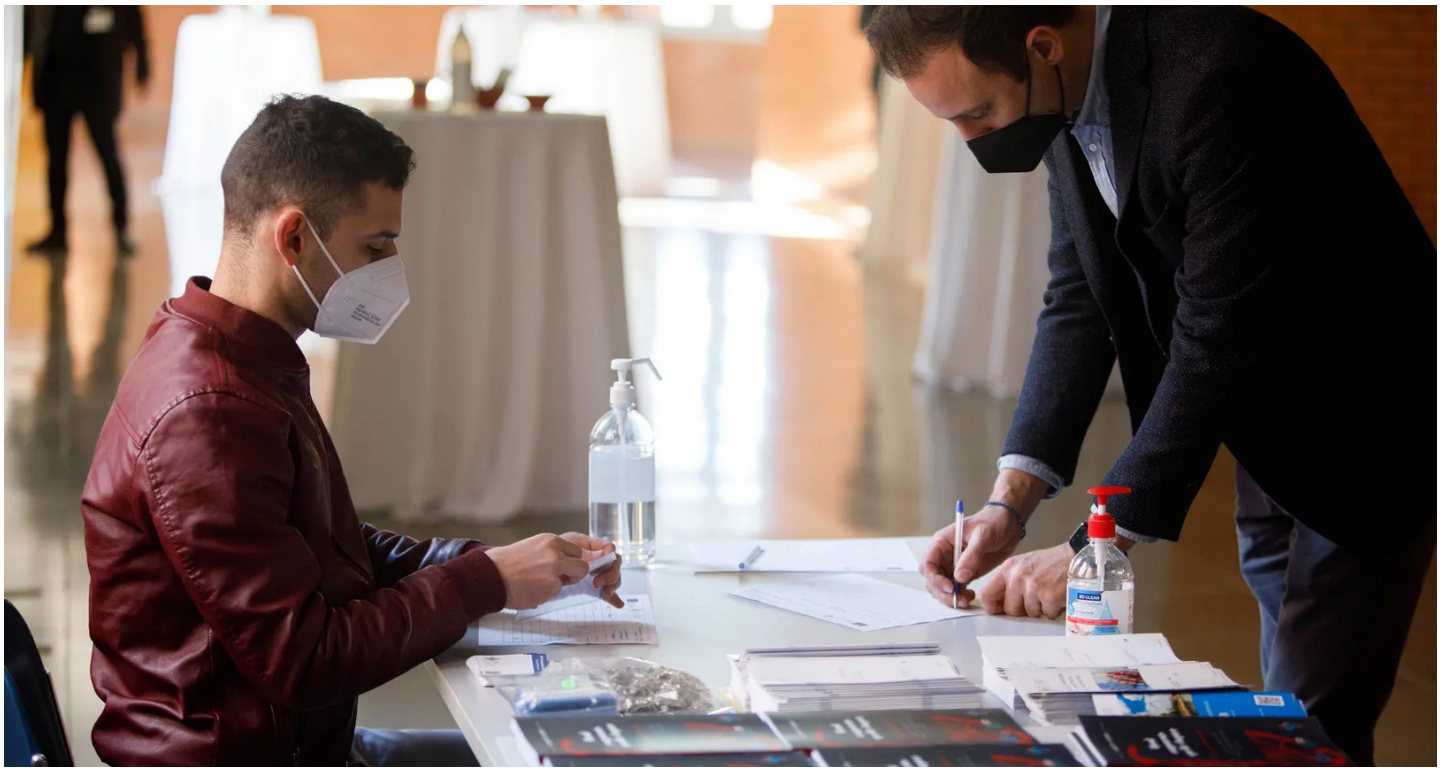
This brochure is part of the joint action '785269/GAPP' which has received funding from the European Union's Health Programme (2014-2020)

Final Dissemination Conference

The website was further enhanced in view of the Final Dissemination Conference, hosting a dedicated section with the development of tailored content and materials. Key items included:

- the Agenda for the two days
- the press release including quotes by the European Commission and GAPP JA Coordinators
- a tailored presentation, developed jointly with the WP leaders providing at-a-glance, an overview of the GAPP JA
- an infographic about GAPP JA which was developed to describe in an easy way what the Action is all about
- related material regarding the revision of the BTC legislation
- GAPP JA position statement, and an infographic which was developed to describe in an easy way the Action's messages on BTC policy
- An audio-visual gallery providing images, a sneak-peek video, and links to some indicative coverage generated
- The Action's final Layman brochure (D2.6), and newsletter (D2.3)

A dedicated hashtag #GAPPJA2022 was attributed for the event.



#GAPPJA2022 Highlights

The GAPP JA Final Conference exhibited great participation by experts joining from EU & non-EU countries. During the two-day conference highlighted:

The need to bridge scientific advances with policy, with the focus on patients and donors

- GAPP JA proved to be an important EU funded Action achieving all goals, thanks to the effort of the Consortium, providing a valuable contribution to the EU setting. Furthermore, through the Action Blood, Tissues and Cells Competent Authorities gave strong support/feedback EU Commission
- the continuous innovations in the BTC sector and how legislation lags behind innovation, with great changes to be expected in the sector, with the future full of innovations
- the upcoming Revision of the BTC legislation by the EU Commission, placing the focus on strengthening oversight, facilitating innovation and managing supply issues
- how novel products and processes push the borderlines between regulatory frameworks at both EU and National level
- challenges in the field which include regulatory, technical, financial aspects and resources as well as issues on privacy and the application of the GDPR, interoperability, and linking databases and data collection and reporting lines/systems, in a timely fashion along with the need for benchmarking, and applying an EU-wide approach
- that there's wide heterogeneity and diverging interpretation across Member States, and the need for harmonization
- the need to ensure donor care and protection, and patient-access to therapies that are safe and sustainable

The need for knowledge-sharing, training and further funding

- the need for systematic evidence-based methodology in the field
- the need and the wish for more knowledge sharing, independent research, education and
- training, increasing funding and resources, the further use of existing accreditation
- mechanisms, including the notion of certification which would be better accepted.
- Furthermore, Member States are interested in cooperation & adoption of GAPP JA methodology and training for Competent Authorities, including assessors, inspectors, and train-the-trainers course
- Additional funding would be beneficial to implement concepts developed

The need to apply a holistic cross-sectoral approach and continuation to GAPP concepts in BTC practice, therapies and treatments

- GAPP JA guidance is an important milestone for the improvement of practices and the safety of BTC recipients in EU
- how GAPP has provided strong contribution regarding a risk-based approach, introducing the concept safety, quality, efficacy and cost-effectiveness, along with the use of clinical data and donor follow-up
- the eagerness by members and participants to see the implementation and continuation to the work delivered by GAPP JA in practice

This brochure is part of the joint action '785269/GAPP' which has received funding from the European Union's Health Programme (2014-2020)

GAPP Joint Action Position Statement

on medical treatments & therapies based on blood, tissues and cells

01

Significant **scientific and technological developments** in the blood, tissue and cell (BTC) sector **enable**:

- improved or **novel processing** and testing **protocols**
- novel and innovative **applications**

However, such advancements, may pose a **quality and safety risk** and have a **direct or indirect impact** on the clinical outcome of the recipients (into which BTC are transfused, transferred, injected, grafted or implanted).

02

- the widespread use of SOHO in new developed therapies, and
- the need to call for a legislation able to cover borderline competences

opened a possibility to **fill a regulatory gap** with the revision of the BTC Directives

03

GAPP Joint Action aims at providing EU Competent Authorities (CA):

- with **tools** for the authorization of new procedures for preparation processes at Blood and Tissue Establishments (BTEs), and
- establish **harmonization in the authorisation of novelties** in the field across the EU

04

The discussion among CAs on BTC indicates:

- Member States welcome the creation of an **EU list** of national inspectors/assessors with specialized/senior expertise that could be invited to join or support national inspection systems
- There is a large shared view on the need to have an **upfront risk-assessment as starting point**, to:
  i) assess and authorize novel BTC preparation and
  ii) collect clinical outcome data
- Some MS welcome the proposal to have an **EU-level exchange tools** to optimize the use of BTC amongst MS.

05

GAPP Consortium believes the new BTC Directive should:

- address
  i) the aspects of **technological innovation** and
  ii) its **regulatory framework**
- **provide CA with the mandate** to be informed about any innovation related to BTC products (to perform the preparation process authorization (PPA))
- **provide access to CA to information** related with the evaluation of clinical assessment and follow-up of clinical outcome, in order to:
  i) support CA evaluation and
  ii) PPA to ensure BTC safety and efficacy
- achieve **clarity and transparency** across regulatory borderlines
- include **requirements** to collect and evaluate clinical outcome data
- **adapt dynamically** to rapid technological innovation through continuously updated Technical Guides to achieve quality and safety of blood and tissues and cells

06

GAPP Consortium believes The European Commission:

- takes into duly consideration the possibility **to establish a new Advisory Board** supporting the CAs in the **evaluation** of new blood, tissue and cell products
- could **work together** with already established working groups under the scope of other EU Directives (e.g. IVD, medical devices, ATMP/medicinal products)

Co-funded by the Health Programme of the European Union

This infographic is part of the project/joint action '785269/GAPP' which has received funding from the European Union's Health Programme (2014-2020). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains.

Additional Dissemination activities by GAPP JA Collaborating & Associated Partners

WP1 – provided tissue and cells professionals an update on GAPP JA project in October 2021, distributed GAPP JA materials at the Italian National Transplant Network in November 2021, and conducted a meeting for Competent Authorities in February 2021 in Italy Rome.

WP3- conducted an internal meeting with 15 experts from diverse disciplines at the Ministry of Health; Department of Transplantation and Biomedicine, Sector for Health Inspection, Department of Biomedicine Inspection, Department of Pharmaceutical Inspection in Croatia.

WP5 – provided a face-to-face training in October 2021 to almost 90 experts and HPCs at the Executive Agency Medical Supervision in Bulgaria

WP8 – provided in June 2021 a short online webinar at ESHRE Campus to 230 attendees. Similarly, in April 2021 at EBMT 2021 through its online e-learning platform. In March 2021 WP8 provided an internal training to 40 attendees BST Staff members, and in October 2021 provided together with FIMEA representative a virtual meeting to CAs on Tissues and Cells.

WP9 – provided in September 2021 together with and at Fraunhofer Institute the Video: Concept and demonstrator of the GAPP online platform. In December 2021 the Demonstrator is planned to be presented online at Fraunhofer Institute.

AEBT partner - disseminated GAPP deliverables/outcomes to its 75 AEBT staff members through its online platform. While in February 2021 jointly with WP8 leaders presented to 60 staff members at AEBT online Congress.

Position Paper by GAPP JA
A position statement was prepared by the Consortium in the first quarter of 2021 on the **Public Consultation by the European Commission on blood, tissues and cells (BTCs) for medical treatments and therapies** and with regard to the upcoming **Revision of the Union legislation on BTCs** which is expected during the first quarter of 2022.

Furthermore, the GAPP JA is mentioned in the **EU Evaluation Questionnaire of the EC Open Consultation**, and the intention of the Action has been:

- to contribute to the discussions at the EU level
- to stress the work accomplished so far
- to highlight aspects/elements that need to be taken into account as these were identified within the Action, while also
- taking into consideration the impact on the preparation process authorization and the overall outputs by GAPP JA

EP Magazine – distributed to EP/MEPs (TBC)

Invitation to Transform Alliance MEP Interest Group meeng for June 2022 to discuss the regulatory framework for ATMPs, taking into account the proposed revision of the BTC legislaon.

EHA Collaboraon Plaza –June 2022 Congress

This brochure is part of the joint action '785269/GAPP' which has received funding from the European Union's Health Programme (2014-2020)

CNT and CNS are thankful to the international societies who supported GAPP activities and are still active in the promotion of its outcomes, to all WP leaders, beneficiaries and collaborative stakeholders - as well as the EAB members - for the significant and major effort constantly placed to contribute to the achievement of the Joint Action objective.

Visit our website at www.gapp-ja.eu
Follow us on Facebook (@GAPPjointAction) or Twitter (@GAPPja)

This brochure is part of the joint action '785269/GAPP' which has received funding from the European Union's Health Programme (2014-2020)



GAPP PROJECT

GRANT AGREEMENT NUMBER - 785269
May 2018-April 2021

Web: www.gapp-ja.eu
Email: info@ gapp-ja.eu

GAPPjointAction || GAPPja

Co-funded by
the Health Programme
of the European Union

This document is part of the Joint Action "785269/GAPP" which has received funding from the European Union's Health Programme (2014-2020). The content represents the views of the authors only and is theirs responsibility; it cannot be considered to reflect the views of the European Commission and/or the Consumer, Health, Agriculture and Food Executive Agency or any other body of the European Union. The European Commission and the Agency, do not accept any responsibility for use that may be of the information it contains..