DELIVERABLE 8.4

19 APRIL 2021

FACILITATING THE AUTHORISATION OF

PREPARATION PROCESS FOR BLOOD, TISSUES AND CELLS

Date of submission:	**19 April 2021 (Final version)**
Work package (WP):	WP8
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Deliverable:	D8.4: Data model of information on clinical outcome of application of human blood, cell, and tissue therapeutics
Dissemination level:	Public

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Contents

1. Purpose and scope

The aim of the present document is to define the **structure of data** and **contents** required to provide data and information associated with the clinical components of the Preparation Process Dossier (PPD).

The data model proposed aims to assist the work of

- GAPP WP5 which will further develop template application form for Blood Establishments (BE) and Tissue Establishments (TE) when submitting information to Member States' (MS) Competent Authorities regarding novel Blood, Tissues and Cells (BTC) and changes in preparation processes
- GAPP WP9 which will further develop and integrate these contents into an online platform, thus building a practical tool to support a complete preparation process authorisation (PPA) and to share knowledge on PPA, between European Competent Authorities (CA).

The present document focuses on the data model of information related with clinical components of the PPD.

Other aspects of the authorisation process, namely, BTC characterization, preparation process evaluation and testing requirements will be addressed in the deliverables of other technical Work Packages within the GAPP Joint Action (JA).

2. Guidance and references

In order to develop the clinical component of the data model for a European knowledge-sharing platform that can support CA in the assessment and evaluation of novel BTC or changes in preparation processes of BTC, the WP8 followed the guidance provided by:

- The contents previously produced by WP8: ***Catalogues of existing clinical data*** *and* ***risk-based set of criteria*** *appropriate to provide information on the quality and safety of human blood, cell, and tissue therapeutics* (Deliverables 8.1 and 8.2, respectively) and the ***Methodological framework to evaluate clinical data*** *requested for authorisation processes upon introduction of innovation* (Deliverable 8.3);

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- The **T&C Database** structure and contents proposed by the **EuroGTP II Project** - Good Practices for evaluating quality, safety and efficacy of novel tissue and cellular therapies and products (EuroGTP II Guide).

3. General principles

The structure and contents of the data model were defined with the aim to:

- Harmonise the structure of information on the BTC therapies;
- Support the collection of efficacy, safety and quality data associated with the clinical use of BTC at European level;
- Ensure the consistency with WP9 deliverables.

The level of detail foreseen in the current data model was defined considering:

- The practical use of the online platform;
- The procedures required to enter data by the applicants and/or CAs;
- Relevance of the information/reports that can be extracted and shared once the online platform database is functional and used by the different MS.

The future GAPP online platform will include information submitted by the applicants and CAs as part of the application process to the CA.

By using the GAPP online platform, CA can obtain information e.g. on minimum information of the clinical component of the PPD, level of risk, as well as Clinical Follow-Up Plans (CFUpP) and Clinical Investigation Plans (CIP) for novel BTC therapeutics and changes in preparation processes.

The data model proposed assumes that all non-confidential data related with PPA can be seen/analysed by all CA.

Different levels of access to the information should be further defined by the WP9, according to the purpose and confidentiality levels of the data.

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4. Description of contents

Applicants need to submit information for:

- Section 1, every time if they have a novel BTC or a change in preparation process;
- In addition to Section 1, also Section 2, if they have a novel BTC or preparation process with risk level *low, moderate or high*;
- In addition to Section 1 and 2, also Section 3, if they have a novel BTC or preparation process with risk level *moderate or high*.

Additional information the Figure 1/Section 2 in Deliverable 8.3 (GAPP Technical Annex 3 to overall guidance: assessing clinical data as part of Preparation Process Authorisation).

Applicant should enter information into the second column. CA assessor should enter information into the last column.

Mandatory fields Optional Fields Conditional fields

1. Minimum information of the clinical component of the PPD			
Field name	**Information provided by the applicant**	**Additional information**	**Assessor's comments**
BTC characterisation	A clear characterisation and definition of the BTC under evaluation		
Key clinical benefits of the innovation, if applicable			There is clinical justification for the innovation: □ Yes □ No Comments/open text:
Alternative therapies or BTC, if any			
Clinical indications	Pathologies/conditions that can be treated or prevented with the BTC in question; Including code according to the International Classification of Diseases (ICD) (https://icd.who.int/en)		
Novelty in clinical indication/target group	□ Yes □ No		
The scientific rationale behind the proposition of a new clinical indication; and information on the earlier clinical indication	Open text	Field available only when the option "Yes" is selected in the prior field.	Scientific rationale is acceptable: □ Yes □ No
Supplementary information – Clinical indications	Open text – details of clinical indication		
Potential contra-indications	Open text		
Level of risk	Negligible, Low, Moderate, High Open text/attachment: risk assessment results	The level of risk determines the requirement of the Clinical Investigation Plan (CIP) and Clinical Follow-up Plan (CFUpP) associated	Risk assessment has been performed correctly, takes into account all relevant aspects and is acceptable: □ Yes □ No

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		with the BTC (see data structure section). When risk is negligible, CIP and CFUpP are not required; When the risk is low, CFUpP is required; When risk is moderate or high, CIP and CFUpP are both required.	Comments/open text:
Risk assessment date	When was the risk assessment performed – Date (format example: DD/MM/YYYY)	This date can also be found from the risk assessment document itself, if uploaded on the platform.	
Relevant bibliography	Open text/attachment: literature search protocol (names of databases, search terms etc.), the literature search report, references		Literature search protocol acceptable: □ Yes □ No Literature search report acceptable: □ Yes □ No Relevant bibliography provided: □ Yes □ No Comments/open text:
Other additional data	Open text/attachment: references to work of peers, technical reports, unpublished data etc.		Additional data is acceptable: □ Yes □ No Comments/open text:
Notify Library references	Open text, for relevant Notify Library Record ID(s)	Link to the Notify Library to be added in the platform.	
Application/implant methods	□ Infusion □ Application □ Surgery □ Laparoscopy □ Insemination □ Other(s)		
Specific application/implant methods	Open text	Field available only when the option "other(s)" is selected in the prior field.	
Special skills or training required for application/ administration of BTC	□ Yes □ No		
Details of skills and training required	Open text	Field available only when the option "Yes" is selected in the prior field.	Training plan and/or other actions in place: □ Yes □ No
Administration form(s), concentration(s) and dosage(s) of the BTC (if applicable)	Open text		
Immediate pre-application/ implantation preparation procedures	Open text (description of e.g. adding solutions/ reconstitution procedures, cutting, thawing, auxiliary devices required, if any)		

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2. Clinical Follow-up Plan (CFUpP)			
Field name	**Information provided by the applicant**	**Additional information**	**Assessor's comments**
Clinical Follow-up Plan	Attachment		
Number of BTC applications/recipients planned to be included in the clinical follow-up; statistical methods and rationale used to determine the number of applications/recipients needed	Numerical value; Open text		Number of applications/recipients for follow-up justified and acceptable: □ Yes □ No Comments/open text:
Duration of clinical follow-up and justification for it	Numerical value (length of follow-up of each recipient in days, months or years) Additional open text/comment		Duration of clinical follow-up is justified and acceptable: □ Yes □ No Comments/open text:
Planned follow-up procedures	Open text (description of e.g. tests, samples, imaging; including description of methodology for clinical data collection)		The recipient monitoring/visits is sufficient: □ Yes □ No Relevant and sufficient targets are monitored: □ Yes □ No Procedure of collection, storage and future use of biological samples (if applicable) is defined and acceptable: □ Yes □ No Comments/open text:
Planned data consistency assessment and/or data analysis including biometrics, statistics	Open text		Plan for data consistency assessment and/or data analysis is sufficient and acceptable: □ Yes □ No Comments/open text:
Specific safety parameters defined for follow-up and data collection	□ Yes □ No		
Detailed safety parameters	Open text	Field available only when the option "yes" is selected in the prior field.	Relevant and adequate safety aspects will be followed up and data collected: □ Yes □ No Comments/open text:
Specific efficacy parameters defined for follow-up and data collection	□ Yes □ No		
Detailed efficacy parameters	Open text	Field available only when the option "yes" is selected in the prior field.	Relevant and adequate efficacy aspects will be followed up and data collected: □ Yes □ No Comments/open text:

Clinical follow-up results and conclusions	Open text/Attachment	Can be submitted to CA later	Clinical follow-up results and conclusions are justified and acceptable: □ Yes □ No Comments/open text:

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3. Clinical Investigation Plan (CIP)			
Field name	**Information provided by the applicant**	**Additional information**	**Assessor's comments**
Clinical Investigation Plan	Attachment		
Objectives and purpose of the clinical investigation	Open text		Objectives and purpose of the clinical investigation are justified and acceptable: □ Yes □ No Comments/open text:
Number of BTC applications/recipients planned to be included in the clinical investigation; statistical methods and rationale used to determine the number of applications/ recipients needed	Numerical value; Open text		Number of applications/ recipients for follow-up justified and acceptable: □ Yes □ No Comments/open text:
Multicentre investigation	□ Yes □ No		
List of centers and countries involved in the clinical investigation	Open text		Comments/open text:
Inclusion criteria	Open text		The inclusion criteria are defined and acceptable: □ Yes □ No
Exclusion criteria	Open text		The exclusion criteria are defined and acceptable: □ Yes □ No
Control treatment used	□ Yes (recommended for BTC with high level of remaining risk) □ No	Control treatment recommended for BTC with high level of remaining risk.	
Details of control treatment (incl. randomisation, if applicable); Rationale of not using control treatment, if applicable	Open text		The use of control treatment or not using control treatment is justified and acceptable: □ Yes □ No Randomisation procedure acceptable: □ Yes □ No
Recruitment procedures and informed consent protocol for the recipients	Open text Optional attachment (informed consent form)		Recruitment procedure acceptable: □ Yes □ No Information about the clinical investigation provided to recipients: □ Yes □ No Informed consent procedure acceptable: □ Yes □ No
Planned follow-up visits and procedures	Open text (description of the sequence and details of all investigative procedures, including tests, samples, imaging etc.)		The frequency of recipient monitoring/visits is sufficient: □ Yes □ No Relevant targets are monitored: □ Yes □ No Procedure of collection, storage and future use of biological samples (if applicable) is defined and acceptable: □ Yes □ No
Duration of the recipient participation	Numerical value (length of participation of each recipient in days, months or years)		Duration of recipient participation is justified and acceptable: □ Yes □ No Comments/open text:

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Specific safety parameters defined for clinical investigation	□ Yes □ No		
Detailed safety parameters	Open text	Field available only when the option "yes" is selected in the prior field.	Relevant safety aspects will be followed up and data collected: □ Yes □ No
Specific efficacy parameters defined for clinical investigation	□ Yes □ No		
Detailed efficacy parameters	Open text	Field available only when the option "yes" is selected in the prior field.	Relevant efficacy aspects will be followed up and data collected: □ Yes □ No
Endpoints of the clinical investigation	Open text		Endpoints are justified and acceptable: □ Yes □ No Comments/open text:
Methods for data collecting	Open text (E.g. review of medical records, registries, investigation report forms, patient reported outcome measures (e.g. questionnaires, diaries), samples, imaging; please specify)		Data collecting adequately described and acceptable: □ Yes □ No Comments/open text:
Statistical protocols, data handling, record keeping and methodology for data analysis	Open text/attachment		Data analysis plan acceptable: □ Yes □ No Data storage adequately described and acceptable: □ Yes □ No Comments/open text:
Discontinuation/ termination criteria specified	□ Yes □ No		
Specific discontinuation/ termination criteria	Open text	Field available only when the option "Yes" is selected in the prior field.	Discontinuation/ termination criteria acceptable: □ Yes □ No
Good practices of clinical setting for BTC [adapted from GCP principles] will be followed in conducting the clinical investigation	□ Yes □ No		Comments/open text:
Independent Ethics Committee (IEC) decisions/opinions	Attachment		Favourable decision/opinion exists: □ Yes □ No Comments/open text:
Patient insurance has been acquired or already exists for this clinical investigation	□ Yes □ No Optional attachment (proof of insurance)		Adequate insurance exists: □ Yes □ No Comments/open text:
Appendices e.g. • agreement between BE/TE and clinicians/institutions • CVs of Principal Investigators	Attachment(s)	Possibility to upload several attachments	Appendices adequate and acceptable: □ Yes □ No Comments/open text:
Expected date for final report of the clinical investigation	DD/MM/YYYY	Needs to allow future dates. Add recommendation to the platform: to be reported within one year of completing the clinical investigation (last follow-up procedure of the last recipient).	Comments/open text:

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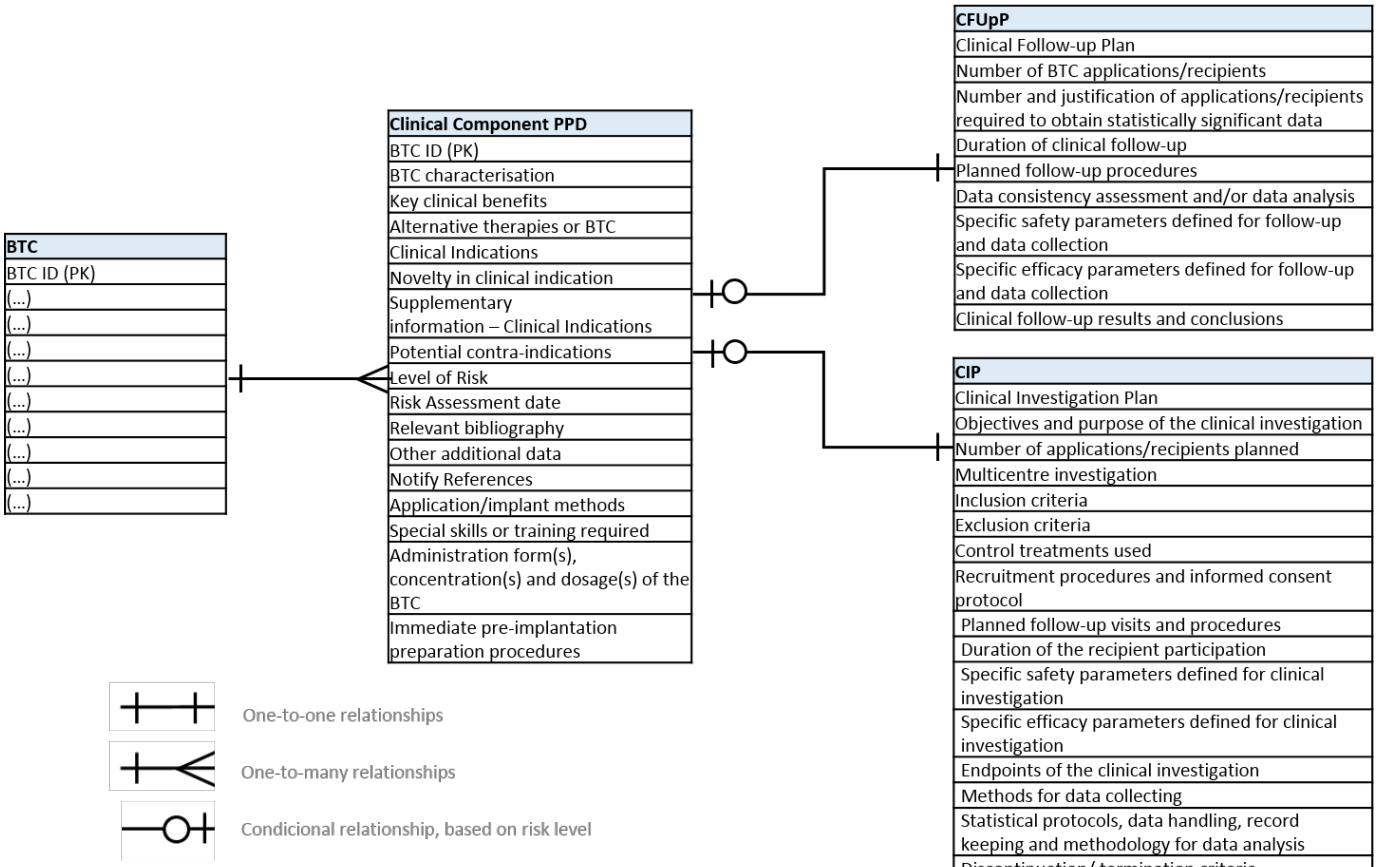
Clinical investigation results and conclusions	Open text/Attachment	Can be submitted to CA later	Clinical investigation results and conclusions are justified and acceptable: □ Yes □ No Comments/open text:

5. Proposed structure of data



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Acronyms

BE	Blood Establishment
BTC	Blood, Tissues and Cells
CA	Competent Authority
CFUpP	Clinical Follow-Up Plan
CIP	Clinical Investigation Plan
CV	curriculum vitae
EuroGTP II	Good Practices for evaluating quality, safety and efficacy of novel tissue and cellular therapies and products (EuroGTP II Guide)
GAPP	Facilitating the Authorisation of Preparation Process for blood, tissues and cells
GCP	Good Clinical Practice
ICD	International Classification of Diseases
IEC	Independent Ethics Committee
JA	Joint Action
MS	Member State
PPA	Preparation Process Authorisation
PPD	Preparation Process Dossier
TE	Tissue Establishment
WP	Work Package

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