CELL HISTORY FILE TEMPLATE

Cell History File – Explanatory Introduction

This template Cell History File (CHF) is a non-mandatory template document intended for establishments and companies involved in the procurement, testing, processing, storage and distribution of human cells and tissues for human application and/or therapeutic use. These could be for autologous or allogeneic use and may include a cell banking step.

The CHF aims to gather the key quality and traceability information required by the EU Tissues and Cell Directive (2004/23/EC) (EUTCD), EU Blood Directive (2002/98/EC) (EUBD) and the EC Regulation on Advanced Therapy Medicinal Products (EC 1394/2007) and is intended to be complementary to documentation required by these legislative texts. In addition, it should satisfy HCT/P requirements in the US.

The view is that this Cell History File could be a '*Cell Passport'* which will accompany a tissue or cell derived product as it progresses through various processing stages. The non-mandatory template aims to provide a model document which developers can adapt to suit their individual requirements, but which will provide a structure that ensures key traceability and manufacturing information is collected and contained in a single source document. It is hoped this document whilst primarily providing a repository of information for various regulatory requirements, will also be useful in any due diligence evaluations.

The template comprises 2 sections (detailed below). The first section covers information on human cells procured for human application.

The second covers the activities that form the starting material for human medicinal product manufacture, regulated under the EC Medicines Directive, 2001/83/EC.

Section A - Human Cell starting material

Section A aims to capture all key information to ensure compliance with the quality and traceability requirements of 2004/23/EC i.e. information on the procurement, testing, storage and distribution of a human cell derived material which can be further processed and used to treat a patient under the EUTCD 2004/23/EC or processed further into a cell line, cell bank, intermediate or final medicinal product regulated under the Medicines Directive 2001/83/EC, all of which will be referred to as *Product* in Section B.

Section B – Cellular product

Section B aims to capture all traceability requirements required for the cell and tissue product from the point when it enters medicines legislation jurisdiction as a Starting Material for a cell based medicinal product. This section aims to capture an overview of the production process including information on the raw materials and reagents used in the manufacture of the product, the testing performed and the storage and distribution of a product.

Use of the Cell History File Template

This template was agreed by a group of Stakeholders in the UK. It aims to provide a flexible format for use by developers and manufacturers of cellular therapy products that will ensure necessary traceability and provenance information is captured in a common source document(s) which can

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accompany the cellular product at each stage of manufacture. The use of the template is voluntary and is supported by the UK Competent Authorities responsible for Human Tissues and Cells, and Blood and Medicinal Products, the Human Tissue Authority and Medicines and Healthcare products Regulatory Agency, respectively.

It is recommended that, wherever possible, the Cell History File accompanies the distribution of a cellular product thereby ensuring the provenance of the cellular product is known to all parties involved in its use or distribution.

It may not be appropriate for an establishment to complete both sections of the template. In such cases the relevant section should be marked as *not applicable* with a brief explanation where necessary.

For some products, for example where a Master Cell Bank is used in the manufacture of multiple final products, it is anticipated that there may be multiple Section B documents.

Where a section is applicable to the product but the information is not available then it is recommended that a risk assessment is performed and documented as appendices to this CHF.

Interaction of the proposed documents with other documents required for ATMPs

The CHF should capture all relevant information of the human cells /tissues used for human application under EUTCD 2004/23/EC or EU BD 2002/98/EC or, in the cases where a Master Cell Bank/Line is produced, as starting material for a human medicinal product under 2001/83/EC.

For human application under the EU Tissues and Cells Directive

In the UK a HTA Preparation Process Dossier (PPD), developed to meet the recommendations of European Union Standards and Training in the Inspection of Tissue Establishments, captures processing, testing and labelling of Tissues and Cells, but does not capture information on procurement, distribution, storage and engraftment. The proposed CHF would dovetail with the PPD and capture all of the necessary information for the production of a human tissue/cell for direct human application (Figure 1).

For use under the EU Medicines Directive (2001/83/EC)

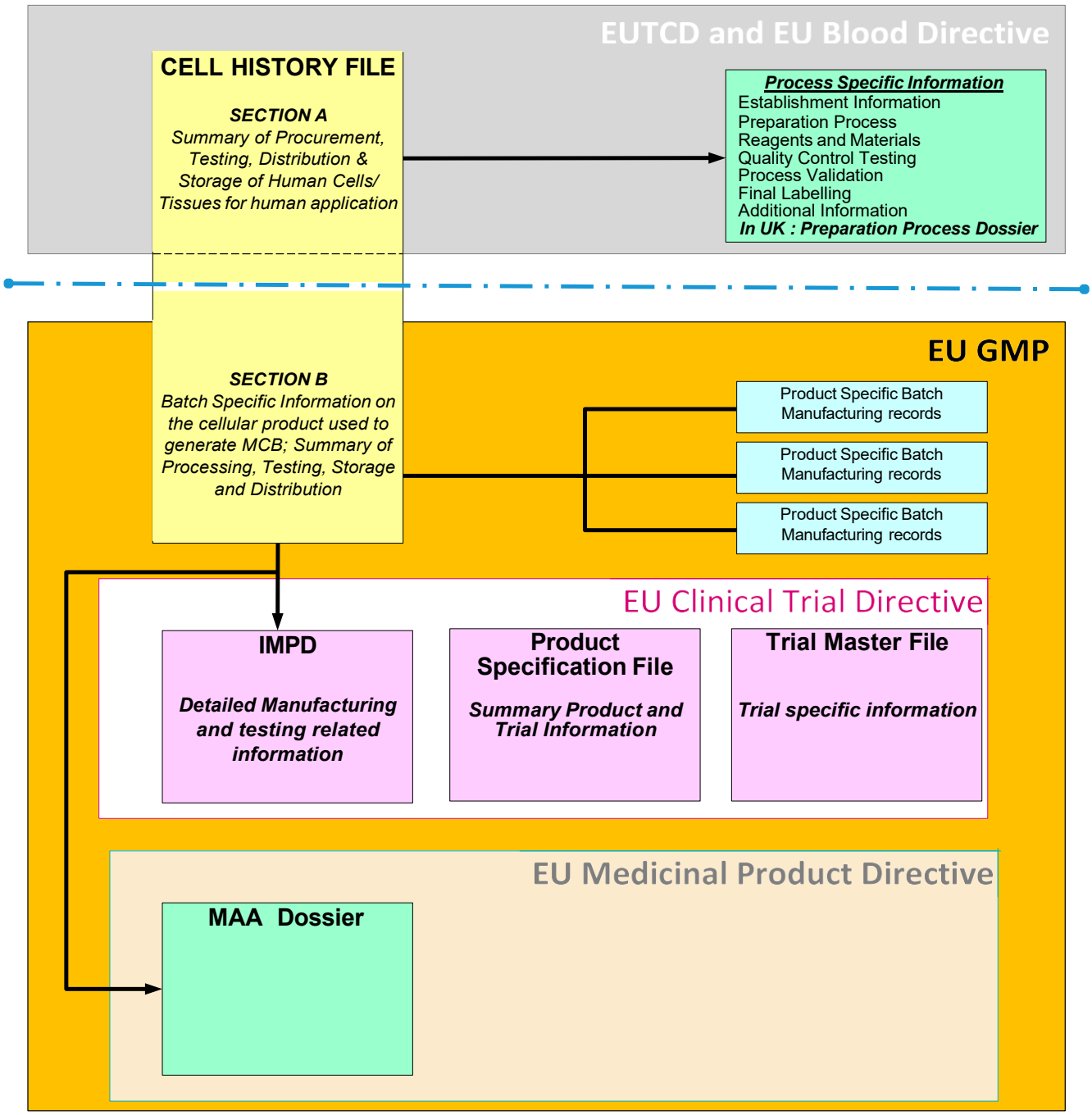
In the EU there are currently a number of regulatory 'compendium' documents which capture some of the downstream processing of human tissues and cells; the Investigational Medicinal Product Dossier (IMPD) for clinical trial products or Marketing Authorisation Application (MAA) and the Product Specification File (PSF) (Figure 1). These documents provide an overview of the production processes which the cell/tissues may have been exposed to. They do not however capture Lot/Batch specific information. As such they do not preserve the record of the history of the tissue/cells started by the CHF.

There is a precedent for capturing data on the bulk starting material which may be used in a number of medicinal products already established in the Active Substance (Drug) master file. Section B of the CHF aims to capture the key quality and traceability requirements for a Master Cell Bank/Cell Line which will be further processed into Human Medicinal Products.

All similar information for processes downstream of the Master Cell Bank (line) should be captured in the individual processing batch records.

It should be permissible for the CHF, if used, to be referenced in IMP and MAA dossiers without the need for duplication.

Figure 1: Interaction of the CHF with other EU regulatory documents



Interaction of international requirements for the processing of Cellular Therapies

This document aims to satisfy the requirements of:

- Directive 2004/23/EC setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32004L0023
- Directive 2002/98/EC setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:c11565
- Directive 2001/83/EC Directive 2001/83/EC on the Community code relating to medicinal products for human use http://eur-lex.europa.eu/legal-content/en/ALL/?uri=CELEX:32001L0083
- ICH Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q5A_R1/Step4/Q5A_R1__Guideline.pdf
- ICH Q5B Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q5B/Step4/Q5B_Guideline.pdf
- ICH Q5C Stability Testing of Biotechnological/Biological Products http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q5C/Step4/Q5C_Guideline.pdf
- ICH Q5D Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q5D/Step4/Q5D_Guideline.pdf
- ICH Q5E Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q5E/Step4/Q5E_Guideline.pdf
- Volume 4 of "The rules governing medicinal products in the European Union" contains guidance for the interpretation of the principles and guidelines of good manufacturing practices for medicinal products for human use laid down in Commission Directives 91/356/EEC, as amended by Directive 2003/94/EC http://ec.europa.eu/health/documents/eudralex/vol-4/
- EMEA/CHMP/410869/2006 Guideline on human cell-based medicinal products http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003898.pdf
- U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research. Points to Consider in the Characterization of Cell Lines used to Produce Biologicals (1993). http://www.fda.gov/downloads/biologicsbloodvaccines/safetyavailability/ucm162863.pdf
- FDA Guidance for industry: characterization and qualification of cell substrates and other biological starting materials used in the production of viral vaccines for the prevention and treatment of infectious diseases: February, 2010. http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/UCM202439.pdf

Cell History File – Template

1 EXECUTIVE SUMMARY

Insert a summary of relevant details of procurement and processing for the various stages of the process:

1) A description of the nature of the tissues or cells, the intended purpose and other key information.
2) Cell history including procurement, testing, storage and distribution (if relevant)
3) Processing to an intermediate, progenitor, master cell line, or master cell bank including a summary of process, testing, storage and distribution (if relevant).
4) storage (short or long term) and the transport system to another organisation (e.g. for later development of a master cell bank or therapeutic product etc).

Illustrations/appropriate flow diagrams can be used as an aid in this summary. Supplementary information e.g. Risk assessment should be appended in the relevant annex.

2 VERSION CONTROL

VERSION	CHANGES	DATE
1.0	N/A, first version of template	29 September 2015
1.1	CGT Catapult branding applied	19 January 2026

Section A INFORMATION ON DONATION/PROCUREMENT OF TISSUES/CELLS

A.1 RELEVANT LEGISLATION

Include details of regulation cells/tissues procured against *e.g., EU Tissues and Cell Directive (2004/23/EC) and additional local requirements*

A.2 DETAILS OF PROCUREMENT ORGANISATION

Information on centres or establishments in which procurement/collection of cells and/or tissues is performed. For each site please include the following general information:

- Name of Contact Person
- Address
- Licence/Authorisation number and any relevant accreditations
- Details of organisation(s) responsible for obtaining consent and where record is held.
- Details of organisation(s) responsible for assessing donor suitability and where details of medical screening and medical history are held (*if different from consenting organisation)*

A.3 DONOR CONSENT

Insert:

1) A copy of a blank Patient Information and Consent protocol.
2) A confirmatory statement that the donor consent has been signed and that consent is in compliance with relevant legislation

A.4 DONOR SUITABILITY

Insert a copy of a blank donor assessment (donor screening and medical history) record including agreed deferral criteria.

A.5 DETAILS OF DONOR TESTING ORGANISATION(S)

Information on centres or establishments in which testing of donor samples is carried out. For each test please include the following general information:

- Testing performed including details of mandatory and additional testing performed
- Name of Contact Person
- Name and Address of testing organisation
- Licence/Authorisation number (if relevant) and any relevant accreditations
- Copy of Specification (if relevant)

A.6 DETAILS OF PROCUREMENT

A.6.1 Donation details

- Quantity and type of cells/tissue
- Donation number (ISBT compatible if available)
- Date of collection/procurement
- Details of collection/procurement

A.6.2 Testing

- Details of testing performed on donor material including methods
- Test results

A.6.3 **Details of any processing and/or cell selection** (if appropriate)

- Selection procedures
- Any processing performed including information on materials and reagents which have been in contact with the cells
- Procedures of quarantine for testing purposes

A.6.4 Storage

- Place of storage *(Name and address of storage facility if different from collection centre)*
- Cryopreservation medium *(where applicable)*
- Storage container materials
- Temperature specification for storage
- Shelf-life *(may change as more data gathered)*
- An inventory should be established and maintained. The fates of the unit should be detailed (*this may be separate from the this Cell History File)*

A.7 CONTRACTS/AGREEMENTS

Include a list of relevant contracts and service level agreements.

A.8 SUMMARY

Include a summary of information outlining any omissions or issues and any mitigation actions (all risk assessments should be contained in Section A Annex 1).

Section A Annex 1 List all risk assessments performed for the cell/tissues. Append a copy or reference the appropriate file/location

Section B – DETAILS OF CELLULAR PRODUCT

A Cellular Product refers to any intermediate of final product e.g. progenitor cell line, master cell bank, intermediate product, final medicinal product. As such it will be necessary to complete separate Section B file for each processing event for the cellular product.

B.1 INFORMATION ON THE CELLULAR PRODUCT

Insert summary details of the cells used to generate the cellular product (if SECTION A not completed/available).

B.1.1 Details of organisation(s) supplying the material for cellular product

Information on centres or establishments in which procurement/collection of cells and/or tissues is performed. For each site please include the following general information:

- Name of Organisation
- Name of Contact Person
- Address

B.1.2 Transfer details

Provide details on the following:

- Purpose of transfer
- Name and address of Establishment/Company where the cells/tissues where obtained from
- Number of units transferred
- Date of transfer
- Date of receipt
- Vessels used in transfer
- Temperature specification for transfer
- Copy of temperature logger printouts
- A statement/information from the users of this document about their systems and practice for maintaining traceability and anonymity requirements throughout.

B.1.3 Information on storage of cells prior to processing

Include information on storage, the date of entry into storage, date of retrieval from storage, storage conditions and verification that correct storage conditions have been maintained during storage period.

B.2 DETAILS OF SUBSEQUENT PROCESSING

B.2.1 Details of processing site

Information on processing centre, include the following general information:

- Name of Contact Person
- Address
- Licence/Authorisation number and any relevant accreditations
- Summary of licenced activities
- Summary of other activities performed

B.2.2 Summary of processing

B.2.2.1 Description of processing

Include a flow diagram and summary narrative including details of passage numbers, derivation and expansion steps and critical controls.

B.2.2.2 Raw Materials used in the production of the Cellular Product

Provide the following details:

- Identification code, manufacturer name and address
- Source and traceability details
- Specification
- Batch numbers and expiry dates
- Compliance with national and/or European specifications *e.g. EDQM Certificate of Suitability*

B.2.2.3 Details of other key materials used in the production of Cellular Product

Provide the following details:

- Storage Container product code, manufacturer name and address
- Batch numbers and expiry dates
- Compliance with national and/or European specifications of all materials *e.g, CE marked*

B.2.3 Details of cellular product(s) generated

Provide the following information on each Cellular Product generated.

- Lot number
- Passage number
- Dates of manufacture
- Quantity and product type (include total amount/volume collected, amount/volume entered into storage, the amount/volume used for testing purposes and the amount/volume discarded)
- Storage details
    - storage materials and conditions
    - Preservatives used
    - Place of storage (name and address of storage facility if different from collection centre)

    - Storage temperature specification
    - Number of units placed into storage (unless recorded elsewhere, Section B Annex 1 should be used as a record of withdrawal of units, this should include date of withdrawal, proposed use of cells and name and address of company/person cell supplied to)
- Date lodged with Stem Cell bank *(if relevant)*
- Stability protocol summary
- A statement/information from the users of this document about their systems and practice for maintaining traceability and anonymity requirements throughout.
- An inventory should be established and maintained *this may be separate from the this Cell History File)*

B.2.4 Analysis of Cellular Product

B.2.4.1 Testing performed on cellular product

Include a description of the methods employed for all analytical testing performed on the cellular product

B.2.4.2 Specification

Include a copy of the approved Specification for the cellular product

B.2.4.3 Batch analysis

Include a copy of results of batch analysis and/or copy of the Certificate of Analysis

B.2.4.4 Details of testing organisation(s)

Information on centres or establishments in which testing of the processed cells and / or tissues is carried out. For each site please include the following general information. In addition please include the following specific information for any testing performed on processed cells/tissues.

- Testing performed
- Name of Contact Person
- Address
- Summary of licenced activities
- Authorisation number and any relevant accreditations
- Copy of Specification

B.2.5 Statement of manufacture

Include a statement on whether the Cellular Product was generated under GMP or Good Tissue Practice, this should be provided by EU Qualified Person wherever possible.

B.2.6 Contracts/agreements

Include list of all relevant contracts/agreements.

B.2.7 Summary

Include a summary of information outlining any omissions or issues and any mitigation actions (all risk assessments should be contained in Section B Annex 2)

Section B	**Annex 1**	**List all risk assessments performed for the cellular product. Append a copy or reference the appropriate file/location**