PPD validation report template

This template has been prepared by the HTA’s Preparation Process Dossier Working Group (PPDWG) to help establishments produce validation reports to fulfil Section E of the Preparation Process Dossier (PPD). Whilst use of this template is not required, it is highly recommended and will facilitate the efficiency of the PPD review process.

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| **Title** |  |
| **Document reference number** |  |
| **Version number** |  |
| **Corresponding Author (name and contact details)** |  |
| **HTA licensing number** |  |

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**Document revision history**

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| **Revision Number** | **Details** |  **Author** | **Date** |
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# 1. Table of contents

Use this section to provide a list of contents with page numbers.

# 2. Background

Use this section to provide information of the product being developed and a summary of how it will be used.

What is the context of the preparation process and the validation? In essence, what is being validated and why?

# 3. Aims

Use this section to provide a brief summary of the aims of the validation.

For example, the aim of the validation may be to provide documented evidence that a preparation process developed in-house can be relied upon to produce a product that:

1. Has not been rendered clinically ineffective or unsafe as a result of the processing; and
2. Has defined critical quality attributes.

Alternatively, the validation may have been conducted to demonstrate in-house operational validation of a published methodology. The report can also be used to demonstrate the suitability of an established preparation process through a retrospective analysis of clinical outcomes.

**4. Critical Quality Attributes (CQAs)**

A CQA is a physical, chemical, biological, or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality.

Use this section to specify the Critical Quality Attributes (CQAs) necessary for you to be satisfied the tissues or cells are not rendered clinically ineffective or harmful by the preparation process. The validation report should precisely define the CQAs and provide information on the tests performed to determine whether the CQAs have been achieved. You must also demonstrate that the process is reproducing the CQAs consistently. You may need validated assays to measure CQAs.

CQA example 1: The CQAs for a cornea may be the density of viable cells per surface area, evidence of freedom from microbiological contamination, and transparency.

CQA example 2: For cell preparations, CQAs may include: the minimum number of cells per unit; a minimum acceptable viability; and a minimum purity of the cells, based on an analysis of the phenotypes in the cell population.

CQA example 3: Where there has been open processing or a decontamination step, include a CQA based on microbiology testing or media-simulation.

You may wish to include a table like the one below as part of this section to provide a snapshot of the CQAs and tests performed.

|  |  |
| --- | --- |
| **CQA** | **How tested** |
| >90% cells viable after processing | Trypan Blue |
|  |  |

# 5. Critical Process Parameters (CPPs)

A CPP is a process parameter whose variability has an impact on a CQA and therefore should be monitored or controlled to ensure the process produces the desired quality.

Use this section to identify the Critical Process Parameters (CPPs) that will bring about or preserve the CQAs. The validation report should specify how the CPPs have been optimised and, where necessary, how their tolerance levels have been set. The rationale for the specified CPPs should be clearly explained.

CPP example 1: For freeze-drying acellular pericardium, residual water and stability of the resulting collagen matrix are defined as CQAs. The temperature and duration of the process are CPPs because they critically impact the CQAs.

Further examples of CPPs: transport times prior to processing, temperature in transit or volume/size of starting material.

You may wish to include a table like the one below as part of this section to provide a snapshot of the CPPs, tests performed and tolerance levels set.

|  |  |  |  |
| --- | --- | --- | --- |
| **Process** | **CPP** | **How tested** | **Tolerance levels**  |
| Freeze drying acellular pericardium | Temperature |  |  |
| Freeze drying acellular pericardium | Freezing time |  |  |

# 6. Experimental design

Use this section to describe the design of the validation studies. It should include a synopsis of the experiments, along with the rationale for choosing the particular materials and methods.

It would be appropriate to include the following for each experiment:

* aim of the experiment
* nature of the samples used, including the number of replicates and details of any controls or reference samples
* who has performed the experiments (for example, your establishment or other collaborators) and rationale for this
* methods used (including any relevant SOPs)

# 7. Results

Use this section to capture the experimental results that demonstrate that the preparation processes described in the PPD produces a product which meets the specified CQAs, including information that supports any CPP tolerance levels set.

The results section is the most important section of the report and it should be where you demonstrate that the tissue and cell processing procedures have been validated, and that they do not render the tissues or cells clinically ineffective or harmful to the recipient. There is no requirement for studies demonstrating clinical effectiveness, though such validation may be acceptable for process authorisation.

Results should be presented clearly, utilising graphical formats where appropriate.

Please note: During the PPD review process, the HTA may request to review the associated raw data.

# 8. Discussion and conclusions

Use this section to discuss the results and to state the conclusions drawn. Include details of future work and monitoring.

# 9. References

Use this section to reference any publications relevant to method development and validation experiments. Please supply full text versions of all key publications.

Please note: During the PPD review process, the HTA may request full text publications if not supplied.