



Technical Report No. 81

Cell-Based Therapy Control Strategy

Currently in preview, click buy full version



PDA Cell-Based Therapy Control Strategy Technical Report Team

Authors

Valérie Pimpaneau, Voisin Consulting, Co-Chair

Jean Stanton, Johnson and Johnson., Co-Chair

Michael Blackton, Adaptimmune LLC

Vijay Chiruvolu, PhD, Kite Pharma

Fabio D'Agostino, PhD, Newcastle University

Margit Jeschke, PhD, Novartis

Michele Myers, PhD, GlaxoSmithKline

Audra Riley, NewLink Genetics

Mercedes Segura, Ph.D., bluebird bio

Contributors

Richard Dennett, Voisin Consulting

Ricardo Jimenez, Lonza Houston, Inc.

Bernadette Keane, PhD, Keane Consulting

Mark Leney, PhD, ClearPath Development Company

Maria del Pilar Redondo, TiGenix

Kirstin Powel, Novartis

Karen Walker, Seattle Genetics

To order this document, please visit: go.pda.org/TR81

Cell-Based Therapy Control Strategy

Technical Report No. 21

ISBN 978-1-945584-06-0

© 2017 Parenteral Drug Association, Inc.

All rights reserved.



Table of Contents

1.0 Introduction.....	1	7.0 CONTROL STRATEGY	25
1.1 Scope and Purpose	2	7.1 Process Parameters Controls.....	26
1.2 Background.....	3	7.2 Material Attribute Controls.....	27
2.0 Glossary and Abbreviations	5	7.2.1 Raw Materials	27
2.1 Abbreviations.....	5	7.2.2 Primary Cells as Starting Materials.....	28
3.0 Product Profile	5	7.2.2.1 Vectors as Starting Materials	29
3.1 Target Product Profile.....	5	7.2.3 Components.....	29
3.2 Quality Target Product Profile.....	7	7.3 Procedural Controls	30
3.3 TPP and QTPP for A-CeT.....	8	7.3.1 Aseptic Manual Processing.....	30
4.0 Critical Quality Attributes.....	10	7.3.2 Personnel.....	30
4.1 Criticality Assessment	11	7.3.3 Environmental Monitoring.....	31
4.2 CQAs for A-CeT.....	12	7.3.4 Facilities and Equipment	32
4.2.1 Visual Appearance.....	12	7.3.5 Advantages to Using Isolators	
4.2.2 Identity	12	and Automation	32
4.2.3 Impurities	14	7.4 Testing Controls	32
4.2.4 Potency.....	14	7.4.1 Product Release Specification	33
4.2.5 Strength/Dose.....	14	7.4.1.1 Identity.....	33
4.2.6 Safety.....	14	7.4.1.2 Potency.....	33
5.0 Critical Process Parameters	15	7.4.1.3 Purity.....	34
5.1 Identification of Process Parameters (Step 1)	15	7.4.1.4 Safety.....	34
5.1.1 Process Mapping for A-CeT	15	7.4.1.5 Dose.....	35
5.2 Parameter Criticality Assessment (Step 2).....	17	7.4.2 In-Process Testing.....	35
5.2.1 Parameter Criticality Assessment for A-CeT	17	7.4.3 Characterization.....	36
5.3 Parameter Risk (or Process Capability)		7.4.4 Process Monitoring.....	37
Assessment (Step 3).....	19	7.5 A-CeT Manufacturing Control Strategy	37
5.3.1 Process Capability Assessment for A-CeT.....	20	7.5.1 Control Strategy Summary for A-CeT	42
5.4 Process Performance Assessment.....	20	7.5.1.1 Material Attribute Controls for A-CeT	42
6.0 Critical Material Attributes	21	7.5.1.2 Procedural Controls for A-CeT.....	43
6.1 Identification of Raw Materials (Step 1)	21	7.5.1.3 Process Parameter Controls for A-CeT.....	43
6.2 Criticality Assessment (Step 2).....	22	8.0 Lifecycle Management	44
6.3 Raw Material Knowledge (or Process Capability)		9.0 Summary	44
Assessment (Step 3).....	23	10.0 References	46

FIGURES AND TABLES INDEX

Figure 1.0-1	Process Flow Diagram for A-CeT	2	Table 6.2-1	Raw Materials Impact Classification.....	22
Table 3.1-1	Points to Consider for the Development of the TPP	6	Table 6.2-2	Process Reagents Criticality Assessment of Culture Expansion Step on A-CeT CQAs ...	23
Table 3.2-1	Points to Consider for QTPPs.....	8	Table 6.3-1	Occurrence Scoring for Raw Materials.....	24
Table 3.3-1	Sample TPP for A-CeT.....	9	Table 6.3-2	Detection Scoring for Raw Materials	24
Table 3.3-2	Sample QTPP for A-CeT	9	Table 6.3-3	Quantitative Impact of Process Reagents for Culture Expansion Step on A-CeT CQAs	25
Table 4.1-1	Impact (Severity) Assessment.....	12	Figure 7.0-1	Schematic Control Strategy Development	26
Table 4.1-2	Criteria for Uncertainty Scoring of Product Attributes	12	Figure 7.0-2	Specific Elements of Control Strategy Components	26
Table 4.1-3	Product Attribute Criticality Assessment.....	12	Figure 7.3.3-1	Foundation for Environmental Monitoring Program	31
Table 4.2.3-1	Example Criticality Assessment Results for A-CeT.....	13	Table 7.4.3-1	Examples of Characterization Testing.....	36
Table 5.1.1-1	IPO Diagram for A-CeT Cell Culture Expansion Step	16	Table 7.5-1	Implementation of Risk-based Tools for A-CeT	38
Table 5.2-1	Process Parameter Severity Scoring	17	Figure 7.5-1	Decision Tree for Parameter or Material Criticality Assessment (PMCA)	38
Table 5.2.1-1	Parameter Criticality Assessment for Culture Expansion Step of A-CeT CQAs.....	18	Figure 7.5-2	Decision Tree for Parameter Capability Assessment.....	38
Table 5.3-1	Criteria for Occurrence Assessment	19	Table 7.5-2	Example of Elements of the A-CET Control Strategy for Safety CQA.....	39
Table 5.3-2	Criteria for Detection Assessment	19	Table 7.5-3	Testing Plan for A-CeT	42
Table 5.3.1-1	Quantitative Impact Process Parameters of Culture Expansion Step on A-CeT CQAs	20	Figure 9.0-1	Overarching Strategy for Risk-based Approach	45
Figure 6.0-1	Assessments Required to Contribute to Overall Raw Material Control Strategy	21	Figure 9.0-2	Control Strategy for Critical Quality Attributes	45
Figure 6.1-1	Materials Used in the Manufacturing of an Autologous Cartilage Cell Product.....	22			