



# **Technical Report No. 81**

## **Cell-Based Therapy Control Strategy**



[www.pda.org/bookstore](http://www.pda.org/bookstore)

## **PDA Cell-Based Therapy Control Strategy Technical Report Team**

---

### **Authors**

---

<b>Valérie Pimpneau</b> , Voisin Consulting, Co-Chair	<b>Margit Jeschke</b> , PhD, Novartis
<b>Jean Stanton</b> , Johnson and Johnson., Co-Chair	<b>Michele Myers</b> , PhD, GlaxoSmithKline
<b>Michael Blackton</b> , Adaptimmune LLC	<b>Audra Riley</b> , NewLink Genetics
<b>Vijay Chiruvolu</b> , PhD, Kite Pharma	<b>Mercedes Segura</b> , Ph.D., bluebird bio
<b>Fabio D'Agostino</b> , PhD, Newcastle University	

### **Contributors**

---

<b>Richard Dennett</b> , Voisin Consulting	<b>Maria del Pilar Redondo</b> , TiGenix
<b>Ricardo Jimenez</b> , Lonza Houston, Inc.	<b>Kirstin Powel</b> , Novartis
<b>Bernadette Keane</b> , PhD, Keane Consulting	<b>Karen Walker</b> , Seattle Genetics
<b>Mark Leney</b> , PhD, ClearPath Development Company	

**To order this document, please visit: [go.pda.org/TR81](http://go.pda.org/TR81)**

# **Cell-Based Therapy Control Strategy**

**Technical Report No. 81**

ISBN: 978-1-945584-06-0  
© 2018 Parenteral Drug Association, Inc.  
All rights reserved.



[www.pda.org/bookstore](http://www.pda.org/bookstore)

# Table of Contents

<b>1.0 Introduction.....</b>	<b>1</b>	<b>7.0 CONTROL STRATEGY .....</b>	<b>25</b>
1.1 Scope and Purpose .....	2	7.1 Process Parameters Controls.....	26
1.2 Background.....	3	7.2 Material Attribute Controls.....	27
<b>2.0 Glossary and Abbreviations .....</b>	<b>5</b>	7.2.1 Raw Materials .....	27
2.1 Abbreviations.....	5	7.2.2 Primary Cells as Starting Materials.....	28
<b>3.0 Product Profile .....</b>	<b>5</b>	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
<b>4.0 Critical Quality Attributes.....</b>	<b>10</b>	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 and Automation .....	32
4.2.2 Identity .....	12	7.4 Testing Controls .....	32
4.2.3 Impurities .....	14	7.4.1 Product Release Specification .....	33
4.2.4 Potency .....	14	7.4.1.1 Identity.....	33
4.2.5 Strength/Dose.....	14	7.4.1.2 Potency .....	33
4.2.6 Safety.....	14	7.4.1.3 Purity.....	34
<b>5.0 Critical Process Parameters .....</b>	<b>15</b>	7.4.1.4 Safety.....	34
5.1 Identification of Process Parameters (Step 1) .....	15	7.4.1.5 Dose .....	35
5.1.1 Process Mapping for A-CeT .....	15	7.4.2 In-Process Testing.....	35
5.2 Parameter Criticality Assessment (Step 2) .....	17	7.4.3 Characterization .....	36
5.2.1 Parameter Criticality Assessment for A-CeT .....	17	7.4.4 Process Monitoring.....	37
5.3 Parameter Risk (or Process Capability) 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
<b>6.0 Critical Material Attributes.....</b>	<b>21</b>	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		
6.3 Raw Material Risk (or Process Capability) Assessment (Step 3).....	23		
		<b>8.0 Lifecycle Management.....</b>	<b>44</b>
		<b>9.0 Summary .....</b>	<b>44</b>
		<b>10.0 References .....</b>	<b>46</b>

## FIGURES AND TABLES INDEX

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