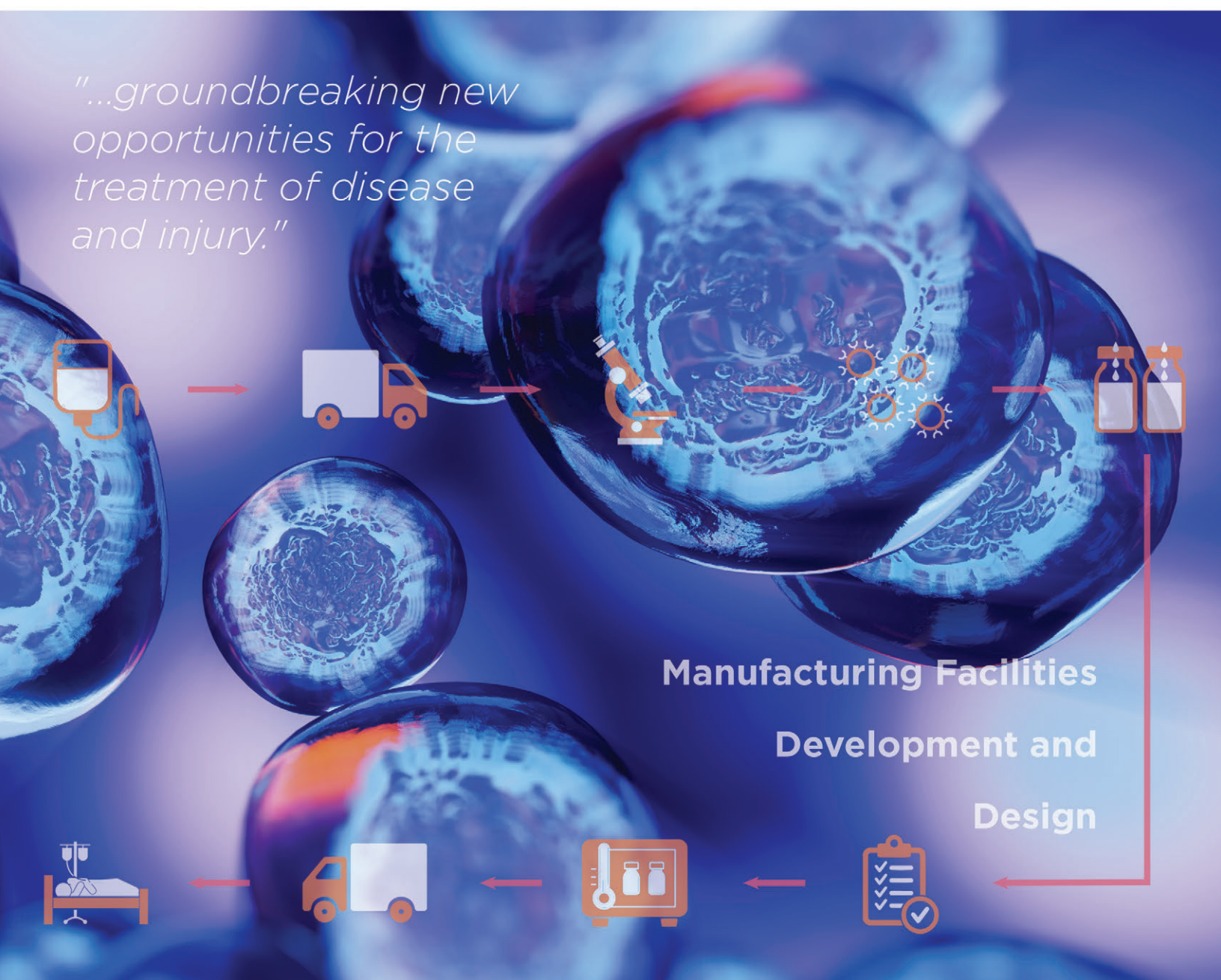




GUIDE:

Advanced Therapy Medicinal Products (ATMPs) Autologous Cell Therapy

"...groundbreaking new opportunities for the treatment of disease and injury."



Manufacturing Facilities

Development and

Design



GUIDE:

Advanced Therapy Medicinal Products (ATMPs) Autologous Cell Therapy

Disclaimer:

This Guide is intended to assist with manufacturing facilities development and design for producing autologous cell therapies. This Guide is solely created and owned by ISPE. It is not a regulation, standard or regulatory guideline document. ISPE cannot ensure and does not warrant that a system managed in accordance with this Guide will be acceptable to regulatory authorities. Further, this Guide does not replace the need for hiring professional engineers or technicians.

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Preface

In March of 2018, the Steering Committee of the ISPE Biotechnology Community of Practice (CoP) submitted a Guidance Document proposal for this first of its kind Guide for ATMPs. The vision of the mission was to expand the growing body of knowledge of this life-changing platform for what was referred to as “personalized medicine” in the industry. We had no idea of the events that would unfold in the months ahead and how the journey would end.

The goal of the Guide is to provide current best practices addressing the key design and operational challenges for the commercial manufacture of ATMPs under cGMP. The rapid pace of change within the ATMP space is unprecedented in the industry. Science and regulatory guidance is being expanded and challenged on what seems like a monthly basis. As it is today, the rapid growth of the product pipeline creates opportunities for life-changing therapies along with significant challenges that must be addressed.

Developing a new guidance document for industry in “normal” times takes a lot of effort from very talented and dedicated professionals. Building on the current ISPE body-of-knowledge, creating new content, and delivering that content during a global pandemic required even more from this special group of people. This Guide, the first of a set of ATMP-focused guidance documents, introduces the ATMP platform and focuses on Autologous Cell Therapies.

On behalf of ISPE, the Biotechnology and ATMP CoPs, and the Members of this Guide Team, we hope this document becomes both a reference for those entering the ATMP space and the first of a growing number of guides expanding the industry’s knowledge of this life changing therapeutic platform.

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The Guide was produced by a Task Team led by Jeff Odum, CPIP (NC Biosource, USA). The work was supported by the ISPE Biotechnology Community of Practice (CoP).

Core Team

The following individuals took lead roles in the preparation of this Guide:

Tom Bannon	PM Group	Ireland
Vince Cebular	IPS – Integrated Project Services	USA
Pinar Cicalese	Immatics	USA
Bruce Davis	BD Global Consulting	United Kingdom
Lesley Davis	Project Farma	USA
Norman Goldschmidt	Genesis AEC	USA
Christoph Herwig	Vienna University of Technology	Austria
Niranjan Kulkarni, PhD	CRB	USA
Brian Pochini	Sanofi	USA

Chapter Writers and Reviewers

The Lead and Core Team wish to thank the following individuals for their valuable contribution during the preparation of this document.

Phil Baratta	Project Farma	USA
Erich Bozenhardt	United Therapeutics	USA
Jose A. Caraballo	Kite Pharma, a Gilead Company	USA
Andrew Doppstadt	Project Farma	USA
Paul Fleming, PMP	Roche Genentech	USA
Emilie Pelletier	Iovance Biotherapeutics	USA
Prof. Dr. Christa Schröder	Fakultät Life Sciences	Germany
Aaron Weinstein	IPS – Integrated Project Services	USA

Other Contributors

The Team wish to thank the following individuals for their significant contribution to the document.

Arantxa Lera Anton	PM Group	Ireland
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Regulatory/Subject Matter Expert Input and Review

Particular thanks go to the following for their review and comments on this Guide:

Martine Powell Senior GMDP Inspector	MHRA	United Kingdom
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The Team would like to thank to Robert Dream, PE, CPIP (HDR Company LLC, USA) for supporting and mentoring the team authoring this Guide.

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Company affiliations are as of the final draft of the Guide.

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600 N. Westshore Blvd., Suite 900, Tampa, Florida 33609 USA
Tel: +1-813-960-2105, Fax: +1-813-264-2816

www.ISPE.org

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1 Introduction

1.1 Background

Advanced Therapy Medicinal Products (ATMPs) are based on genes, cells, or tissues delivered to patients to provide a therapeutic benefit based on a specific target of interest. For ATMPs, the therapy is cells, engineered tissues, or the manipulation of the patient's genome. This is in contrast with traditional manufacturing processes for compounds that are synthetically derived (i.e., small molecule) or proteins or peptides expressed by cellular systems (i.e., large molecule biopharmaceuticals).

There are two general primary focus areas for ATMPs:

- **Cell therapy** products are manipulated whole living cells, sometimes using gene therapy methods that are introduced into the patient and act at the cellular level to treat disease or injury. There are two categories of cell therapy products:
 - Autologous: Cells are derived from a patient and returned to the same patient after *in vitro* manipulation.
 - Allogeneic: Samples are derived from donors and the final cell therapy can be used to treat many different patients.
- **Gene therapy** refers to a rapidly growing field of medicine in which genes are introduced into the body to treat or prevent diseases. Gene therapy active substance contains recombinant nucleic acid that will regulate, repair, replace, add, or delete a genetic sequence in the patient. Although a variety of methods can be used to deliver the genetic materials into the target cells and tissues, modified viral vectors represent one of the more common delivery routes because of their transduction efficiency for therapeutic genes.

These general definitions encompass a wide spectrum of products and treatment methods with unique manufacturing challenges that must be supported by appropriate facility designs. ATMPs often treat rare diseases with unmet needs, or dramatically improve upon existing therapies, so there are strong social and financial drivers for rapid commercialization. Once approved however, future process, equipment, or scale-out changes require regulatory re-approval, so designing scalable and preferably automated manufacturing processes with robust control strategies is necessary to mitigate the commercial supply risk.

This Guide acknowledges that the term ATMP is quite broad (e.g., allogeneic and autologous cell therapy, gene therapy, and tissue engineering) and that these are emerging therapies utilizing rapidly evolving technology and equipment. In recognition of this, this Guide covers autologous cell therapies for parenteral use while providing content that may be applicable to other types of ATMPs.

1.2 Scope and Purpose

This Guide focuses primarily on manufacturing facility development and design for autologous cell therapies for parenteral use.

The following areas are not in the scope of this Guide:

- Manufacture of autologous cell therapies for non-parenteral use
- Tissue-based autologous products
- Implanted autologous products