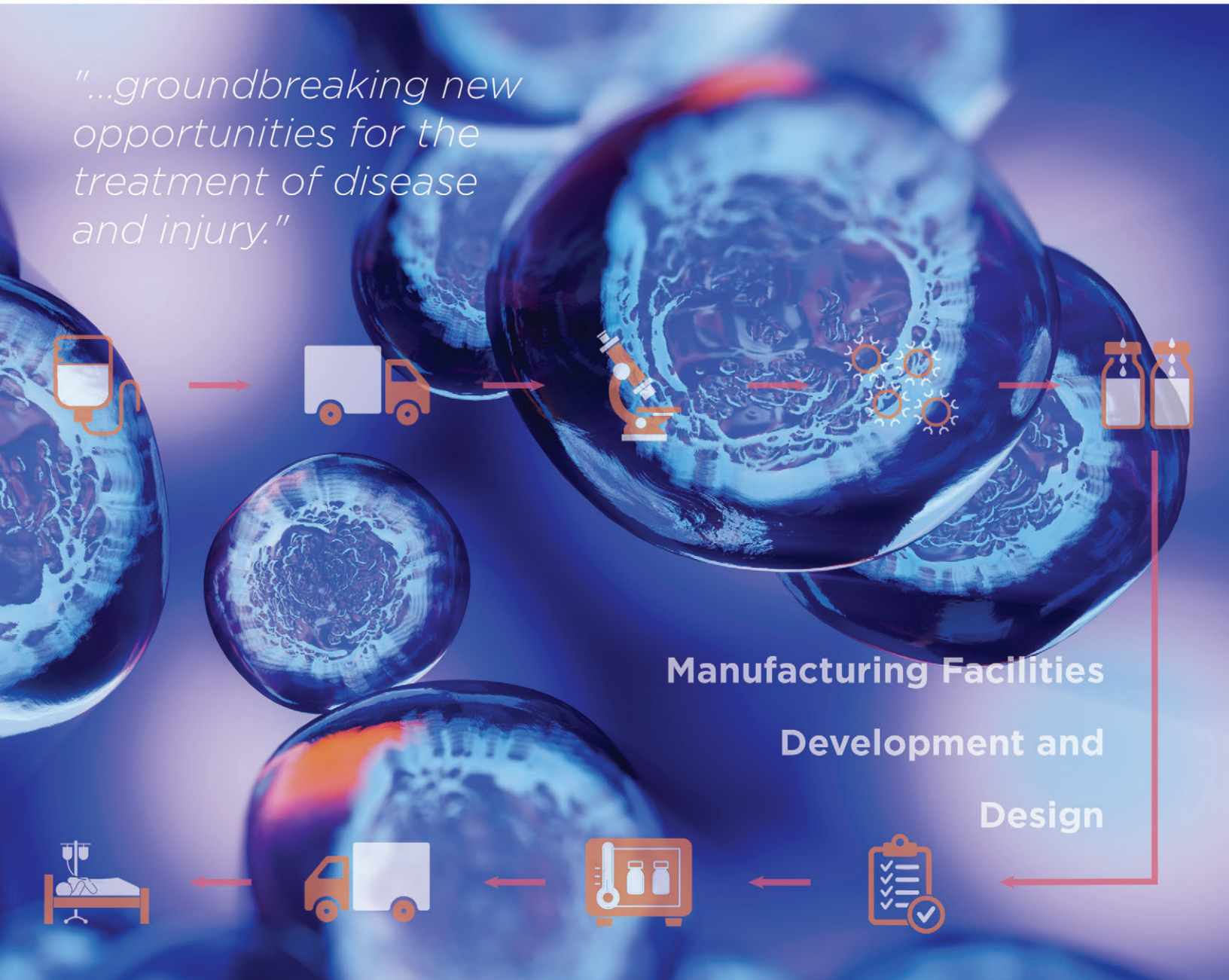
ISPE®

GUIDE:

Advanced Therapy Medicinal Products (ATMPs)

Autologous Cell Therapy



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Autologous Cell Therapy

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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.

Acknowledgements

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).

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The Leads would also like to thank ISPE for technical writing and editing support by Nina Wang (ISPE Guidance Documents Technical Writer/Editor) and production support by Lynda Goldbach (ISPE Publications Manager).

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

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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