

FOREWORD

Time to move away from the ‘process is your product’ paradigm?

Chris Mason & Elisa Manzotti

As cell and gene-based therapies move through the development pipeline towards the clinic, manufacturers are faced with a number of challenges pertaining to the move from clinical-stage bioprocessing to commercial-scale manufacturing. One of the critical questions centers around the implications of making process changes as you move towards commercialization and how can you control for these variables and the potential risks they introduce. For many years now within this sector it has been commonly accepted that “your product is your process”, but as we continue to take strides in developing our understanding of both of these facets, will we start to see a move away from this paradigm?

This spotlight, which is **Part 3 of our Cell and Gene Therapy Manufacturing series**, features articles from leading experts from industry and academia who are working to tackle this question and look at solutions to the current challenges of process and product development within manufacturing. Working with our expert Guest Editors – **Dr Gregory Russotti** (Celgene Cellular Therapeutics, USA), **Dr Stephen Ward** (Cell Therapy Catapult, UK), and **Dr Peter Zandstra** (Univ. Toronto, Canada), we hope you’ll find this spotlight engaging and importantly, help push the discussion forward so that the industry can continue its path towards commercial reality.

Product & Process Understanding

Our spotlight is led by an article on manufacturing process development of ATMPs within a regulatory framework for EU clinical trial & marketing authorisation applications. The quality attributes of advanced therapy medicinal products that correlate with safety and efficacy in patients are determined not only by manufacturing process inputs such as starting and raw materials, but also by how the manufacturing process itself is designed and controlled. **Giulia Detela** (Cell and Gene Therapy Catapult, UK) and **Anthony Lodge** (Chiesi Farmaceutici, Italy) describe how the critical quality attributes and analytical requirements can be incorporated

into the design of industrialized ATMP manufacturing processes to support effective regulatory submissions in the EU.

We hear from the frontline in our Innovator Insight article from **Dan H O'Donnell** (Director of Cell Therapy Logistics, Fisher BioServices, USA) who provides critical insight into the key factors that contribute to the commercial success of ATMPs, in particular, of autologous immunotherapies. He discusses the challenges involved in process development and logistical considerations for these cell-based products.

Continuing our **Future Leader** series, we're delighted to feature a perspective article on "Quality-by-Design" (QbD). With many cell and gene therapy companies struggling to meet the manufacturing demands of large-scale commercial production, the industry is slowly moving towards implementation of QbD principles to gain an understanding of the impact of critical process parameters on critical quality attributes of the product. **Fernanda Masri** (CCRM) provides insight on how ultra scale-down approaches can be utilized as a tool to enable a QbD approach to cell and gene therapy manufacturing.

Automation: Migration from Manual Processes to Closed-System Automation

Some of the key drivers for process changes and development as you move from early-stage through to commercial-scale manufacturing are the need to demonstrate consistent reproducible quality of product and, as we often hear in the industry, the necessity to drive down the cost of goods. Transitioning to automated platforms and systems is one approach to achieving this goal but at

what stage in process development should you first consider automated systems and what impact can you expect automation to have on cost, quality and reproducibility? These are not straightforward questions to answer and therefore we wanted to give due consideration to this important topic by inviting leading experts in automation to share their experience and provide insight into the latest developments automation technology.

First we hear from our Automation **Guest Editor, Qasim Rafiq** (University College London and Aston University) and **Robert Thomas** (Loughborough University, UK) about the evolving role of automation in process development and manufacture of cell and gene-based therapies. They discuss how the early integration of automation facilitates process transitions at later stages of clinical development and commercialization, and address the need to balance this with minimizing capital expenditure early in your product's development.

Leading on from this, we hear from a leading industry expert, **Brian Hanrahan** (Invetech, USA) who shares his extensive experience and discusses the key factors that can influence automation decisions in cell & advanced therapy manufacture.

Following on from **Nicholas Medcalf's** excellent article in Part 1 of our spotlight discussing the different business models in cell and gene therapy manufacturing, the conversation moves on to how advances in technology and integration of automated production platforms have the potential to support decentralized manufacturing. **Richard Harrison** (Aston and Loughborough University, UK), **Qasim Rafiq** (University College

London & Aston University) & **Nicholas Medcalf** (Loughborough University) recognise that in order for decentralized manufacturing to succeed, effective procedures for managing and automating procurement of starting materials and consumables, tracking of work in progress, release of product and overall administration must be prepared.

In the final piece in our Automation Spotlight, **Michael Kulik, Jelena Ochs, Niels König** (Fraunhofer Institute for Production Technology, Germany) and **Robert Schmitt** (Aachen University, Germany) discuss the potential of automation of cell manufacturing to provide robustness and adaptivity of your processes. Applying the principles of Industry 4.0, they share their vision of how production engineering concepts can be translated in order to address the challenges arising within the manufacturing of therapeutic cell products.

We hope you enjoy the Cell & Gene Therapy Insights – Spotlight on **Product and Process Understanding & Automation: Migration from Manual Processes to Closed-System Automation** – you can access all content free of charge on the CGTI website, in addition to a host of other useful content, videos and webinars in our **Manufacturing Resource Center**.

Chris Mason

*Chief Science Officer,
AvroBio Inc., 400 Technology Square
Cambridge, MA 02139, USA*

Professor of Regenerative Medicine Bioprocessing, UCL, London UK

Elisa Manzotti

*CEO and Founder, BioInsights
e.manzotti@insights.bio*