Biomanufacturing & Cell and Gene Therapy

Insights from the Industry

BIOMANUFACTURING

CELLANDGENETHERAPY

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Introduction

There are few years in living memory as disruptive and uncertain as 2020 has been. While this is true of almost every sector, the events field has seen unprecedented change in how events are held and how operations will be conducted in the future.

Proventa International was among the companies spearheading this innovation, utilising its trademark versatility to ensure that none of its important meetings were cancelled and its mission was carried out. Moving fully online, Proventa was able to facilitate connections and host expert, sector-critical discussions that would otherwise have been missed.

Despite the unforeseen challenges 2020 brought, Proventa's meetings were as successful as always, bringing together top-tier industry experts to talk through challenges and innovations with one another, make new connections and take back brand new information to their companies. Whatever challenges the rest of the year brings, those who attended the online meetings will be able to face them fully prepared and as informed as possible.

The Future of Biomanufacturing and CGT

While not quite as affected by the recent pandemic as some areas - for example clinical trials - manufacturing is currently entering a fascinating new era of technological growth and change. The roundtables held by Proventa this year took advantage of this, discussing among other things innovations and new methods for effective downstream viral inactivation; how to succeed in digital transformation; and the opportunities and challenges in manufacturing bioreactors based scape-up.

From downstream manufacturing to GMP manufacturing to single-use technologies, Proventa's October 2020 event looked at some of the most relevant and important changes in the field today, with leading experts offering their insights and thoughts to those who were there.

This report will look at some of the highlights of the recent Biomanufacturing and Cell and Gene Therapy events, but will also go further: it will explore what delegates are investing in right now, and look ahead to the next five years in the field: how Biomanufacturing and CGT will change as the years roll on, and how delegates are being affected by the turbulence of Covid-19.

We hope you enjoy this report, and look forward to seeing you at our events next year,

Joshua Neil, ***Editor***
Proventa International

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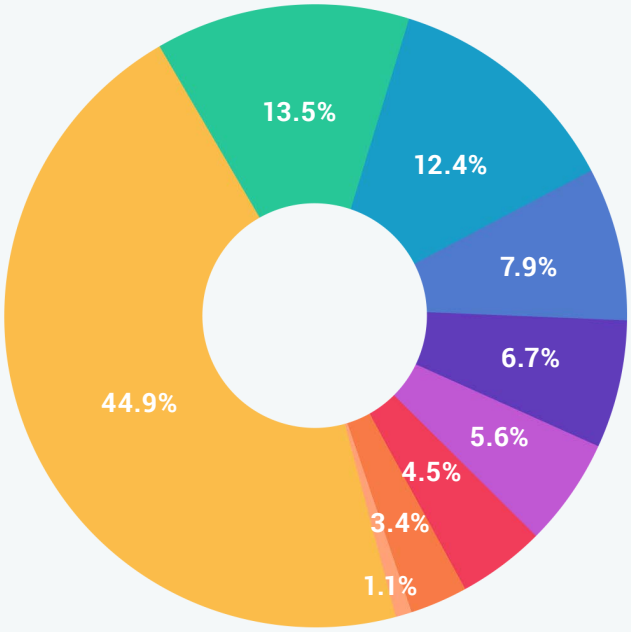


44.9% Director Level

13.5% Scientist

12.4% Department Head

7.9% President / VP

6.7% Other

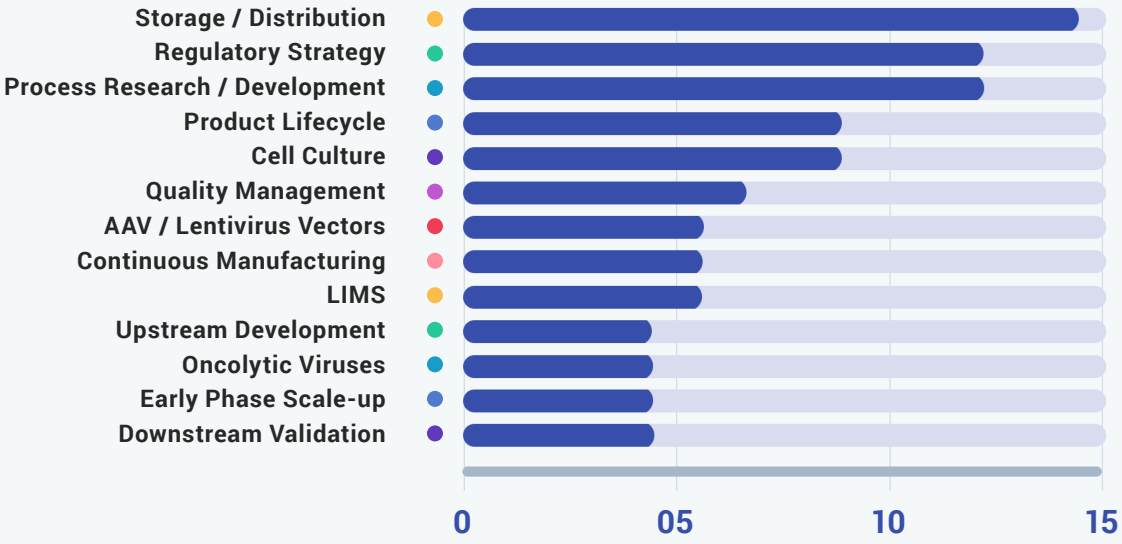
5.6% Team Lead

4.5% C-level

3.4% Manager

1.1% Academia

Key Investments



2020 Event Highlights

BIOMANUFACTURING

Single-Use Systems / Next Generation Biomanufacturing Facilities

A fascinating roundtable was held early in the morning on single-use technologies, looking at next generation biomanufacturing facilities and facilitated by **Mohamed Chtaini, Executive Director of Global Commercial Biologics Manufacturing at Incyte**.

The roundtable focused on the new wave of single-use technologies, for example bioreactors, mixers, bags for solution preparation, and single-use transfer lines among other things.

Chtaini began by noting that regular manufacturing facilities have transfer lines, CIP skids, tanks to be purchased: these have a long lead time. Single-use manufacturing facilities, by contrast, have low cutbacks and greater time saved. There is also greater flexibility, as equipment can be moved around. This means the facility can be adapted to the product. As a closed system, there is no need to worry about cleaning validation, steaming validation etc.

Delegates also pointed out other benefits to single-use technology: that such facilities come fully installed, and when coupled with ready-made media you can simply plug-and-play to begin.

One issue with the technology that delegates pointed out, however, related to the environmental effect. There were a number of studies mentioned that pointed out the cost and waste in producing plastics as opposed to the traditional method. Chtaini added that when talking to plastic suppliers, they mention that companies are still saving on water and detergents etc, which have a major impact on the environment, and stainless suppliers would say the same thing. An independent study must be done to deal with this, he noted. Luckily not all plastic generated is a waste: in the US, there is a company collaborating with biotechs on the East Coast that bring in plastics and recycle it to make materials for roads, to get materials for pallets, etc.

On recycling, one delegate mentioned that he could understand recycling for bags of bifur not in contact with biotherapeutics / biomolecules, but not for any recycling of single-use products when it has been in contact with their target molecule - there is never another solution than burning anything, due to confidentiality and patient/environment safety. Delegates discussed this, and noted that the materials could be burned in factories that make electricity from this; and also that this is only the beginning of single-use systems being used in the industry. As they proceed, they will see ways of dealing with the waste.

The next topic related to how delegates were impacting their GMP modules, and how they were handling giving control to someone else. Chtaini pointed out stainless steel bioreactors, once bought, were in the control of the pharma companies and could be steamed, cleaned, and reused. Switching to plastic bioreactors, however, meant that control is no longer with the pharma companies - they are now made by someone else. Equipment becomes a consumable that must be purchased from the supplier, with pharma needing to ensure that the bag and other materials are being made with the required quality, on time. Supply chains, he said, become vital - and additionally, pharma can only use the equipment of the specific supplier they have chosen.

It was mentioned that this problem increased the need to build partnerships. Following from this, one delegate raised the topic of picking the right supplier. Chtaini and others noted that the industry desperately needs standardisation, as well as increased transparency of the supply chain - often, he said, suppliers are relying on one another. He cautioned delegates to thoroughly audit their supplier, and ensure they're aware of industry standards. He pointed out that the biotech industry in plastics are still small players, but easily the most demanding. It was important to continue this, and make 'a lot of noise' to ensure things continued to change in the right direction.

The session ended with a call to pick suppliers wisely. Chtaini said that the long-term impact of the supplier picked could not be underestimated, and that this had a big impact on any facility.

Overcoming Problems Associated with Transitioning Manufacturing from Early-Phase to Late-Phase Development

One particularly fascinating discussion around CGT was headed by **Antoine Heron, Site Head/ VP, Global Biologics Manufacturing, Quality, Strategy at Merck**. He began by mentioning early phase and drivers of complexity. These included that CGT assets are first developed by an academic institution, and generally that means a limited product knowledge or process/ manufacturing development; angel or venture investment funding, which leads to a focus on financial return and exit strategies; and tight milestones to unlock the next funding tranche, which means that first-in-human supercedes a robust manufacturing strategy with line-of-sight to commercial scale.

One delegate also shared another driver of complexity: whether their product's scaffold, which is an ancillary material and cannot be seen after the harvest, must be fully GMP-compliant and always created in a centralised manner.

Others replied that given this was early development stage, it was not important to streamline at the very beginning of the manufacturing process; it was more critical to move the startup company to the next stage, that is, generating meaningful clinical data from phase 1. They added that so long as the company was capable of producing clinical materials at small scale, even if the process was manual and open, investors would be sufficiently satisfied.

It was then noted that small biotechs often need to go to external manufacturers for their equipment and expertise. This is a huge challenge, and means such smaller companies must think carefully about materials they're using: replacing them with GMP-grade materials could add months to the transition process from clinical academic process to a GMP environment.

Several delegates expanded on this point. One added that during collaborations with academic institutions/hospitals, it's often the case that what's good for a hospital in phase 1 won't cut it for commercial manufacturing. Many changes need to be made, not least in process controls and operator training, where for example there is no close cytometry. He added, however, that complexity issues will go away if a suitable platform could be found of raw material / supply chain / equipment / in process controls / release assays etc, assuming there aren't significant problems with material sourcing or cell lines that refuse to co-operate.

Key Delegate Challenges - 2020 and Beyond

Regulations

The regulatory space topped the list of challenges delegates cited as occupying their thoughts for the near future. This covered the full range of issues within regulation, including the lack of a regulatory framework in some countries, submitting regulatory dossiers in accelerated timelines, non-harmonised regulations and determining the regulatory strategy for a company.

Time and Resource Management

Often a major challenge for delegates, time and resource management once again topped the list of difficulties facing pharma companies in the coming years. Accelerated timeframes and general work timelines were often mentioned, alongside other resource difficulties including resource management and training and technical resources.

Outsourcing and Partners

The third most-cited difficulty facing those who attended Proventa's event related to outsourcing work and partnering with other organisations. Selecting a good CRO/CMO, CMO transfer and quality at CMOs were the main issues mentioned as challenges for the years to come.

Data

A number of issues around data were also high up on delegates' main challenges for the future. Experts at the event specified data analytics, ownership of data and data integrity and QMS integration as vital aspects of the field that need to be overcome for companies to move forward in the near future.

Commercialisation and Competition

The commercial aspects of biomanufacturing and CGT were another factor causing issues for delegates. Experts' difficulties included the transition to commercial biomanufacturing, a competitive marketplace, and transfer and validation of manufacturing processes from R&D to commercial sites to allow for commercial launch.

Key Delegate Challenges - 2020 and Beyond

Hiring and Internal Expertise

Hiring and training were further difficulties experienced by delegates from across the board. Hiring competent staff, training human resources, and finding individuals with CGT expertise were some of the challenges mentioned within the area.

Scaling Up and Scaling Out

The equal challenges - and difficulty choosing between - scaling out and scaling up were also mentioned by delegates. Many companies are still having difficulty choosing between the two options, though solutions continue to appear on the horizon.

New technology

The sourcing and incorporation of new technologies into companies is another challenge that delegates said they faced, though this difficulty was lower on the list than expected. In particular, delegates mentioned the problem of rapid technological evolution making it hard to thoroughly evaluate them for translational approaches, and the discovery of new technologies.

Raw materials

Raw materials were a minor challenge faced by some attending the event, with delegates mentioned challenges around single sourced raw materials, for example sterile custom bags, and the availability of quality raw materials.

Automation

Finally, automation was cited as a difficulty for some, with delegates suggesting that improvements needed to be made with implementation of automation and that a lack of automation in general was a significant hindrance for them.

A Look Ahead:
Biomanufacturing and CGT Over the Next 5 Years

While key investments of our leading delegates are a useful indicator of what is most important to industry professionals both now and in the immediate future, their scope and importance only extends so far ahead. To look further - to the next five years in Biomanufacturing and CGT, for instance - Proventa asked its facilitators about their expectations for the near future, and how the field will have changed in the run-up to 2025.

Digitalisation and AI

Perhaps the most discussed topic during the event was, unsurprisingly, AI and the industry digitalisation surrounding that. One delegate suggested these new technologies have the potential to significantly impact the pharmaceutical bottom line, compared to other industries, and could have a major impact in the next few years. In particular, she said the near future would see increased efficiencies and further automation with reduced losses stemming from this.

Another event attendee agreed with this assessment of the future, suggesting that reduction of overall manufacturing process timeline through automation and virtual reality integration would have a major impact on the manufacturing field. Another delegate seconded this, suggesting that full automation for cell/gene therapies would soon be revolutionising the field.

This area was, however, the area where perhaps the most hype was expected: one delegate noted that misunderstanding what digitalization/AI is and can do could reflect poorly on unprepared companies, while another suggested that overall digital transformation has not been well-defined, with benefits that may well be overestimated.

Continuous Manufacturing and Single Use Technologies

New and innovative processes, such as continuous manufacturing (CM) and single-use technologies, were suggested by some of the delegates as having major importance for the coming years. One delegate pointed out that single-use technology provides flexibility of manufacturing, especially in small batch sizes, while another said the future would see an increase in ballroom concepts (a large manufacturing area with no fixed equipment) and modular manufacturing, disposables, and continuous manufacturing.

A third delegate added to this, saying that to him one of the most interesting developments in recent years has been the ability to manufacture in closed systems.

Cost of Goods and Quality

The cost of goods and of quality were two issues a number of facilitators spoke about. One attendee suggested reducing the costs of quality was an important change to be made over the next few years, while another facilitator suggested the cost of CGT goods as an important factor in the field today.

One delegate noted that there is a consistent focus on cost of goods reduction due to pricing pressures, while raw material control was another major challenge for the next few years - with raw material complexity increasing, there is an increasing need to understand and control raw material variability and supply robustness.

A Look Ahead:
Biomanufacturing and CGT Over the Next 5 Years

Personalised Medicine

One delegate suggested the rise of personalised medicine was one of the most important elements of the field right now, particularly within CGT, due to increasing global demand and progressive sustainability requirements. Another facilitator agreed, stating particularly that personalized medicine supply chain impacts are a huge issue in the field right now. He said that particularly CRISPR, as the 'holy grail of gene treatments', will soon be revolutionising CGT and manufacturing.

A third expert also suggested that from a clinical perspective the rapid rise of CGTs was one of the most interesting developments in recent years, as was the slower pace of CMC innovations in the space.

New Modalities

Introduction and scale-up of new modalities was an expected element of the coming years, according to some of the facilitators surveyed. One facilitator suggested that more approved advanced therapies will change the dynamics of the field, with CDMOs needing to improve their services/ quality or risk companies limiting their outsourcing.

A second expert issued a warning in this area, however, noting the potential for over-exaggeration of the potential of new and untested therapeutics.

Vaccines

The development of vaccines is another area set to change considerably over the coming years. One of Proventa's facilitators said that in recent years, products were developed and generated depending on the market need. So while there was a recent decline in the number of vaccine manufacturers in the U.S., COVID-19 has changed the field and grown vaccine manufacturing considerably. He said the current trend to discover a COVID-19 vaccine has bought up the need of vaccine products, awakening a new interest across the industry globally.

Despite this, another facilitator pointed out that the COVID response could well fall short of expectations, with over 620 trials and no more than a dozen likely winners.

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