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Considerations for the technology transfer of Cell Therapy products. Part 1

This is the first of a series of articles I am writing looking at the technology transfer and industrialisation of gene and cell therapy products. In this part I will give an overview of some of the considerations for the technology transfer of each of the main technology platforms. In future parts I hope to be able to delve into each of these in more detail.

Although there are many similarities, cell therapy products differ from mainstream biopharmaceutical products in that the living cells are the product, not just an intermediary.

There are two main types of cell therapy products: -

Autologous cell therapies are based on cells that are harvested from the patient, cells with the desired properties are isolated and then expanded. The cells are then reintroduced back into the original patient.

Allogeneic cell therapies have cells derived from universal donor cells, which are harvested, isolated, expansion and banking for multiple doses. A single product has the potential to many different patients.

The autologous cell therapies are patient-specific, and as such there is no requirement to increase the scale of the process (scale-up), instead increased production depends on the ability of the organisation to create multiple copies of the same scale process (scale-out). The challenges in the technology transfer of this type of operation lie in the provision of small units capable of quick "product" change around and the provision of high throughput quality control / analytical systems. A considerable degree of flexibility would need to be built into any manufacturing facility for large scale autologous therapy cell production, such a facility will have to be able to cope with great variations in demand.

An upside of this of type of production methodology of course is that "scaling-up scale-out" should be in essence just a repeat of the process already developed and not requiring radical re-design. Prevention of cross contamination will be a major issue but in the whole, should be minimised by the proper use of cGMP procedures. Cost savings due to increases in scale are not possible, however, as the manufacturing process for each "product" can be very similar this type of manufacturing can benefit greatly from the introduction of automated and semi-automated equipment to reduce costs and increase throughput.

One of the main challenges for this type of cell therapy is in dealing with what is intrinsically a variable quality of raw material – the cells from the patient.
Usually this type of therapy is developed in a clinical environment where the patient and the manufacturing unit are in close proximity, they may even be co-located. Technology transfer will in most cases involve the physical relocation of the manufacturing unit, meaning that factors that have never been considered before now have to be taken into account (e.g. effects of transportation time delays, storage conditions – even the need to introduce cryopreservation techniques). These can

introduce significant changes to the processing method and may even require the process to be substantially re-developed meaning studies such as stability need repeating.

Cells for allogeneic cell therapies could be given to many (hundred or even thousands) of recipients and thus this type of cell therapy lend itself to being scaled-up from laboratory bench up to perhaps 2000 litre batch size – or even continuous manufacturing techniques. One of the main challenges in the technology transfer of this process is that cell cultures of this kind are very sensitive to their environment and process scale changes (e.g. from cell culture flask to bioreactor) may be difficult, if not in some cases, impossible. Significant process development will usually be required to both run the process at these scales in the first instance, and to develop the understanding of the key process parameters to control the developed process.

Facilities for scaled up manufacturing often use many of the same techniques and equipment as are found in classical biotechnology products, particularly making use of closed and single used systems such as single use bioreactors. Closed systems are almost essential at the larger scale as downflow booths etc cannot be used and working within cleanrooms with a Class B background incurs significant capital and running costs. Closed systems can safely be used in a Class C environment, and there is an argument for allowing them to be run in Class D environments.

The larger scale operations also provide many opportunities for process optimisation and cost reduction through the development of modular process steps and automation in both production and analytical operations.

As well as a deep scientific knowledge of the product being manufactured, successful technology transfer will also require the use of existing technology transfer methodologies and project management techniques coupled with the application of process optimisation and commercial manufacturing expertise combined with knowledge of facility design, quality, and regulatory systems. For help, talk to us at contact@bluehatchconsultancy.com .

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