[Developing Immunotherapies for Cell-Based vs. Non Cell-Based Therapies](http://blog.fisherbioservices.com/developing-immunotherapies-for-cell-based-therapies-vs-non-cell-based-therapies)

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[Immunotherapies](http://blog.dana-farber.org/insight/2012/06/what-is-immunotherapy-for-cancer/) harness the power of the body's own defense mechanism, the immune system, to combat disease. They were initially introduced in the form of non cell-based biologics and vaccines, such as the splurge of products known as the check-point inhibitors designed to target the [PD1/PD-L1 immune pathway](http://www.onclive.com/web-exclusives/the-role-of-anti-pd-l1-immunotherapy-in-cancer). An individual would be injected with a weakened form of a virus, exposing the body to the disease and prompting the immune system to produce antibodies to fight the infection from the live virus. In recent years, immunotherapies are expanding into the realm of cell and gene therapy. Cell therapy includes [re-engineering the T-cell](http://blog.fisherbioservices.com/clinical-trial-identifies-new-car-t-cell-therapy-to-fight-leukemia) or immune cells and re-delivering these cells back the patient to treat the cancer.

Both cell-based therapies and non cell-based therapies are developed as immunotherapies and therefore they share some similar challenges in development. However, due to the nature of cell-based therapies manufacturing complexities, there are several additional challenges that must be considered. In this blog we'll take a closer look as some of the challenges that cell-based and non-cell based therapies face, and why cell-based therapies are so complex.

**Challenges Associated with Both**

**Enrolling and Retaining Patients**Identifying, enrolling and retaining the right patient population are all essential to the development of therapies. The immune status and genetic makeup of the participants’ cancers are entwined with the development of enrollment and endpoint criteria – selecting the wrong patients or participant dropout halfway through the [clinical trial](http://blog.fisherbioservices.com/cell-therapy-clinical-trials-navigating-the-operational-shift-from-phase-1-to-phase-2) can greatly affect its results.

**Dosing and Measuring Response**One of the greatest challenges in immunotherapy is determining the ideal dosing protocol to elicit the best patient response. Large companies rely on advisors, trials and other resources to determine dosing and measure response while smaller companies usually depend on a single trial.

Another significant challenge is measuring patient response. As of yet, no universal criteria has been adopted to measure immunotherapy response for research or clinical care – many still regard survival as the gold standard for cancer treatment.

**Gauging Patient Reactions**Serious adverse reactions are always possible in immunotherapy trials. Sponsors should always anticipate adverse reactions and remain vigilant for signs of immune-related adverse events (irAEs) and emergent resistance, including chills, fatigue, fever, back pain, nausea, joint ache and headaches.

Sponsors should also look for reactions that do not cause adverse effects. Due to significant patient specificity and durable response even after the end of treatment, cancer immunotherapies can potentially enable an immune response that recognizes and adapts to cancer mutations.

**Challenges Associated with**[**Cell-Based Therapies**](http://blog.fisherbioservices.com/bid/304873/Commercially-Successful-Cell-Therapies-Navigating-the-Ultra-Cold-Chain-Distribution-Minefield)

**Adverse Temperature Events**Adverse temperature events can negatively affect the viability and potency of cell therapies. These types of temperature excursions can occur anytime the material is handled or transported throughout the chain of custody. In fact, any given individual dosage of a cell-based therapy could experience up to eight different adverse temperature events between the time it is removed from storage at the distribution center to the time it is administered to the patient.

**Standardizing Packaging and Distribution**Poor planning in packaging may result in additional handling for storage and distribution, which may lead to higher risk for adverse temperature events and increased production costs.

**Ensuring Consistency Across Clinical Sites**Stocking cell-based therapies at the [clinical sites](http://blog.fisherbioservices.com/bid/371666/Managing-Cell-Therapies-at-Clinical-Trial-Investigative-Sites-Part-1) that use them would be ideal, but managing these therapies requires advanced training for staff and complex storage systems, such as ULT freezers with extra HVAC capabilities and cryogenic storage tanks complete with a steady supply of liquid nitrogen. Only a handful of clinical sites are capable of managing cell-based therapies in an FDA-compliant manner.

**Patient Administration**Some cell-based therapies require complex preparation prior to administration. Site personnel often need additional training in the proper storage, preparation and administration unique to these products; some therapies require additional equipment. Autologous therapies require additional diligence to create a system that properly pairs a patient with the dose.

**Chain of Custody Expertise**Documenting the movement, storage and processing of materials associated with cell-based therapies from manufacture to administration presents many challenges. The [chain of custody](http://blog.fisherbioservices.com/top-10-concerns-and-considerations-in-cold-chain-logistics) must document the movement, handling and temperature of the material at every step in the logistics chain. Furthermore, the chain of custody process must be scalable, consistent from the first phase through commercialization, and comply with 21 CFR part 11 requirements.

Planning for these challenges at the beginning of development of cell-based and non-cell based immunotherapies can reduce the risk for problems in approval, production, administration and tolerance of these therapies.