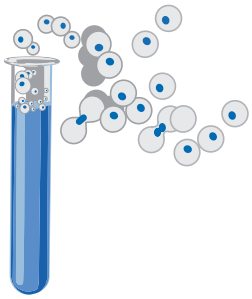
The Novartis Gene Therapies Manufacturing Process

The manufacture of gene therapy is complex. Novartis has developed a reproducible manufacturing process.

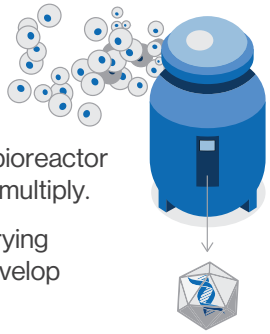
Step 1: Expanding the Number of Cells



The process starts with one vial containing 10 million cells.

For nearly three weeks, they are continuously supplied with fresh nutrients so they can multiply or "expand" in number.

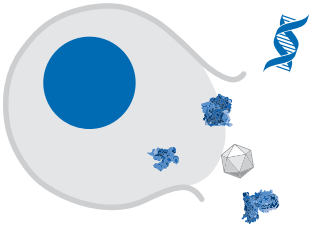
Step 2: Plasmid DNA is Added in the Bioreactor



Once the cells reach 10 billion in number, they are transferred into a bioreactor where they continue to expand and multiply.

Plasmid DNA – genetic material carrying blueprints needed for the cells to develop gene therapies – are introduced.

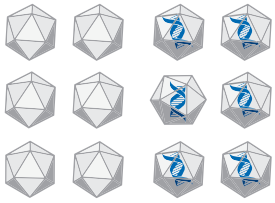
A triple transfection of the cells produces adeno-associated viruses, or AAV vectors, which serve as vehicles to get therapeutic genetic material into a patient's cells. These are known as transgenes and are specifically designed to provide the function of a gene that patients need.



Step 3: Harvest and Filtration

A few days later, the cells are broken open to release the full AAV gene therapy vectors, empty AAV vectors, and other components, like DNA and protein fragments.

Step 4: Filtration and Separation



The product is filtered to remove impurities and meticulously separate the full AAV vectors containing therapeutic genes from the empty ones.

The product is then filtered again to ensure the AAV vectors are sterile and ready for use.

Step 5: Fill and Finish

The product is transferred to vials and inspected for proper fill and closure.

Each time an order comes in, it is custom packed and shipped out within 24 hours.

The AAV platform is robust, which allows for flexibility in downstream purification techniques. The optimal AAV serotype can be chosen for different clinical applications in the future.

NOVARTIS | Reimagining Medicine

The Novartis Standard

Novartis Gene Therapies is committed to manufacturing excellence. Gene therapy can be reliably produced and delivered to patients who have rare and chronic genetic disorders.

Many safeguards are in place to develop safe and high-quality gene therapy. The active lab facilities have ample storage, backup generators, and real-time alarm systems.

For every person involved in the process, there is a second, real-time verifier as well as a quality reviewer. There is also continuous monitoring of all operations and extensive testing throughout production.

Novartis Gene Therapies efficiently produces an uninterrupted supply of gene therapy. Redundant raw-material suppliers are used, and operations run 24/7, 365 days a year.

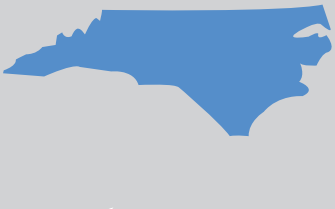
Novartis Gene Therapies has a large, commercially proven gene therapy manufacturing footprint.

This capacity and expertise enables Novartis Gene Therapies to manufacture both currently-approved and pipeline therapies at quality and scale.

Locations

Pilot scale manufacturing site in **San Diego, CA**

Licensed manufacturing site in **Libertyville, IL**



Licensed manufacturing site in **Durham, NC**

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