

HOW NEURO-CELLS® IS MADE

From bloody bags of bone marrow to sophisticated syringes that regenerate futures of people with neurodegenerative diseases

Only a few milliliters of fluid in an injection syringe. That's it. It's a teaspoon of innovative medicine that combats diseases like spinal cord injury and traumatic brain injury. It's the exclusive result of a complex production process in a state-of-the-art facility, performed by people who are committed to walk the extra mile. How does Neuroplast transform a bag of bloody bone marrow into these precious drops of new hope to people with neurodegenerative diseases? Without manipulating or even touching any stem cells? Quality control manager Marco Schaaf, Bouke Albersen from warehousing and manufacturing team leader Inge Corstjens explain everything.

The Neuroplast team delivers fully personalized stem cell treatments for patients that suffer from neurodegenerative diseases. This group of conditions includes traumatic spinal cord injury and traumatic brain injury, but also Alzheimer's or Parkinson's Disease. The goal of Neuro-Cells® is to stop further damage and to optimize healing and regeneration potential.

Before this can happen, many steps have been performed. The patient's stem cells are collected and shipped to the Neuroplast premises. A dedicated team manufactures a living therapy capable of restoring balance to cellular processes. The therapy is then shipped back to the hospital where medical specialists deliver the treatment to the patient.

Exposure of stem cells to the tiniest bit of dust or dander can compromise the entire process. Next to working in cleanrooms, with the typical technology and protocols that go with it, Neuroplast has designed a closed system manufacturing process to keep the stem cells from having any contact with anything whatsoever.

For all of this to work, an incredible amount of expertise, planning, accuracy and teamwork is required. Thankfully, the Neuroplast team is fully equipped for the task.

Quality control manager Marco Schaaf, warehousing associate Bouke Albersen manufacturing team leader Inge Corstjens clarify the process step by step.



Many steps need to be carried out before Neuro-Cells® is ready to be administered to a patient

WHAT ARE NEURODEGENERATIVE DISEASES?

It is estimated that neurodegenerative diseases will impact 115 million people worldwide by 2050. They are conditions to the central nervous system in which important nerves die. Examples are Traumatic spinal cord injury, Traumatic Brain Injury, Frontotemporal dementia, ALS and Parkinson's Disease.

1. Collect stem cells from the patient

After confirming that the patient meets the inclusion criteria and after they have given their consent, medical specialists collect bone marrow from the patient. The doctors use a special temperature-controlled material kit for this, that Neuroplast has shipped to the hospital beforehand. The bone marrow is then shipped to the Neuroplast facilities through specialized couriers. All this time, the temperature needs to remain within a specified range, which is logged continuously.

2. Neuroplast receives the stem cells

By the time the courier arrives at Neuroplast, the team has already collected, cleaned, cleared, documented and prepared the required utilities in MKBs: Material Kit Boxes.

Warehouse associate Bouke Albersen: "These boxes contain all materials that are necessary in the process. We always have one box ready to go, in case a patient needs treatment."

In a special quarantine zone, Bouke selects the needed items for the MKB from large plastic containers with green stickers that say 'ready to use'. Bouke elaborates: "We clean everything vigorously with IPA wipes and special sprays. Even the loose ends of plastic seals."

When ready, Bouke places the material in a hatch. At the other side of this hatch, in the second level of cleanliness, the material is taken out by the biotech associates and cleaned again, with the same rigor.



Material transfers between cleanroom zones via hatches

3. Check bone marrow for quality

Before any manufacturing takes place, the quality of the bone marrow is inspected. Did the transportation go well? Was the temperature constant? Is the bone marrow clot free?

NEURO-CELLS® IS A LIVING THERAPY SUPPORTED BY GROWING CLINICAL EVIDENCE

Neuroplast is a clinical stage stem cell biotech combatting the common cellular processes in neurodegenerative diseases. Neurodegenerative diseases include traumatic spinal cord injury, Alzheimer's, and Parkinson's disease.

Neuro-Cells® addresses the common underlying cellular processes driving neurodegenerative diseases. It is a living therapy that leverages the stem cell's natural abilities to restore balance and interaction of those cellular processes to stop further damage and optimize healing and regeneration potential, that the body itself cannot perform due to the blood-brain barrier.

Neuro-Cells® is tested in an ongoing phase II-III trial for acute traumatic spinal cord injury, and preclinical evidence exists for applications to other neurodegenerative diseases.

Neuroplast holds orphan disease designations for traumatic spinal cord injury and frontotemporal dementia, granting fast-track development towards market authorization and ten-year market exclusivity.

Quality control manager Marco Schaaf oversees the entire process to ensure that the quality criteria are met: "In the absence of any concerns, the bone marrow is cleared to go into production. Thanks to our established protocols for bone-marrow collection and transport, rejection is strikingly exceptional, still thorough checks apply. Via a second hatch, the material now reaches the cleanroom, the third level of absolute cleanliness."

4. Remove red blood cells

Contrary to many other stem cell therapies, Neuroplasts' process is all about eliminating unwanted cells, not about specific cell selection and cell-engineering.

"Typically, manufacturers of stem cell technologies do something with the cells to turn them into treatment. Like cell manipulation, genetic engineering, or culturing cells," Marco states. "Neuroplast works the opposite. We leave what we need alone and take out certain cells that could counteract the desired effect."

The first item on the elimination list: red blood cells.

In the cleanroom, two biotech associates are responsible for production. Manufacturing team leader Inge

Corstjens: "I regularly take on the role as a biotech associate myself. We always work in pairs. One person executes the core manufacturing process. Another person, the witness, documents all steps and performs supporting activities such as checking the volumes."

Inge operates a centrifuge that spins a bag of bone marrow to separate and remove red blood cells. This splitting is done with help of a special gradient, that needs to be added to the centrifuge-kit very carefully. Inge: "We add the gradient to one of the bags of the centrifuge-kit in a biosafety cabinet. This is an extra sterile environment."

Inge continues: "Dependent on the number of cells in the substance, the centrifuging exercise could take around an hour. The machine does the work, but we have to pay close attention to oversee that everything goes according to plan."

If anything does not go according to plan, Neuroplast has prepared fallback options for a multitude of scenarios, including machine failure.

Inge: "We have two of every machine in the lab, that we use alternately. There is always a backup."



In the extra sterile biosafety cabinet, gradients are added to one of the bags of the centrifuge-kit

5. Count the cells

When the centrifuging is done, Inge passes a sample of the remaining fluid to quality control.

Marco: "We have set acceptable ranges for red blood cells depletion and cells that contain DNA, based on prior runs. If the cell counts of the samples fall within these ranges, the fluid is cleared for the next step."

6. Remove immune cells

Not all immune cells are good when you suffer from neurodegenerative conditions. Some of these cell types contribute to inflammation, which, in turn, causes secondary damage to the central nervous system. For this reason, Neuroplast separates these cells from the bone marrow. Again, without touching the cells that are meant for the ultimate therapy.

"We use antibodies that recognize the cells we want to remove," Marco elaborates. "Those unwanted cells stick magnetically, to separate them from the rest of the cell suspension that remains untouched."

Inge emphasizes that this is a new way of using antibodies: "Other pharmaceutical manufacturers typically use antibodies to extract the cells they want to continue working with, and therefore automatically manipulate those cells. We use a reversed approach."

7. Count the cells again

Inge passes another sample to quality control. Based on evidence, Marco knows the exact specifications that must be met in order to continue to the next step.

8. Adjust the volume

Neuro-Cells[®] should be injected directly into the cerebrospinal fluid, to bypass the blood brain barrier and be effective where it is needed: in the central nervous system.

However, at this stage, the cell suspension is too voluminous to inject into cerebrospinal fluid. Therefore, the volume needs to be adjusted. Next to that, the team optimizes the composition of the suspension to keep the cells stable. Inge: "During this wash cycle, we remove what we don't need." The result is a concentrated therapy of the right volume.

9. Check and declare it a therapy

After completion of the last steps in manufacturing, the final product is subjected to testing by quality



The syringe is packed into a special cooling box

control once more and packed for shipment. The bone marrow has now officially been transformed into a therapy: Neuro-Cells[®].

10. Pack Neuro-Cells[®]

Neuro-Cells[®] is put into a special fit-for-purpose syringe. Bouke is waiting in the assembly room to take over.

Bouke: "We pack the syringe into a special cooling box with temperature sensors on it. We insert cooling elements that have followed a very meticulous procedure of freezing and defrosting to ensure the temperature of the syringe is exactly right during transportation."

11. Ship Neuro-Cells[®] to the patient under conditional release

After Bouke has sealed the boxes, he sends Neuro-Cells[®] away to the patient's hospital with a special courier.

Bouke: "It's the end of the production line, but this moment marks the real beginning for the patient."

12. Run quality tests for final release

While the treatment is already underway, the Neuroplast quality control team runs additional tests on

samples to ensure safety and quality on a large list of items, including composition and sterility. In addition, the team runs potency tests, to verify if the product harbors a desired biological activity. All tests are checked by the official qualified person and when all is in order, the treatment is officially cleared for administration to the patient.

13. Deliver the treatment to the patient

The medical staff in the hospital administer Neuro-Cells® into the patient's cerebrospinal fluid.

14. Neuro-Cells® in action

And then finally, it's up to Neuro-Cells® to perform. Once in the body, the living therapy adapts to the patient's specific requirements and restores balance at the cellular interaction level. It aims to modulate inflammation to stop further damage, to restore myelination to improve signal transmission between the central nervous system and the rest of the body, collectively optimizing regeneration potential. Because of all this, patients regain perspective to keep or regain physical and mental function, such as movement, coordination or memory.

It's this perspective to patients that makes all the difference to the Neuroplast team. The long hours of precision work in special clothing, where trivial things like bathroom breaks are kept to a minimum, are small sacrifices to make for such a meaningful contribution to people who otherwise have no outlook on getting better.

Inge: "It's a special job. There are no therapies for the patient groups we work for. It's a great feeling to give people hope that their futures can be better."

WANT TO KNOW MORE?

Neuroplast is always looking for new talent, clinical partners, and investors to accelerate realizing our mission: Using stem cell technology to regenerate futures.

Contact us via info@neuroplast.com or follow us on LinkedIn

