MANUFACTURING OF TISSUE ENGINEERING PRODUCTS FOR REGENERATIVE MEDICINE ACCORDING TO GMP GUIDELINES
With the expertise of scientific project work and the implementation of application-orientated research in practice, we at Fraunhofer IGB focus on the role of a mediator between preclinical research and clinical application for the development of GMP-compliant manufacturing processes for tissue engineering, medical devices and IMPs. Our qualifications are based on longstanding experience in primary cell culture technologies, tissue engineering, regenerative medicine and cell therapy assisted by integration in an excellent network of scientists, engineers and clinicians.

Building on these skills, we at the Fraunhofer IGB develop GMP-compliant processes for the manufacture of individual, autologous tissue replacement for regenerative medicine and its use in clinical studies, we see to applying for the Manufacturing Authorization and produce cell-based therapeutics (ATMPs) in our certified rooms. We are well equipped to support your product pipeline!

Development and manufacture of transplants

One of the focuses of our work is developing biological matrices, for example as vehicles for the manufacture of autologous transplants. We also develop acellular matrices for regenerative medicine, under the Medical Devices Act, e.g. a collagen type I matrix made of rat’s tail tendons or a collagen type I/III matrix from porcine intestine. We establish artificial implants such as stents, heart valves, blood vessel substitutes made of polymer materials with various coatings, for example fibrin. Furthermore, we have developed a melanocyte cell implant for the treatment of vitiligo.

GMP manufacturing unit

Fraunhofer IGB offers services in development and manufacturing of cell-based investigational medicinal products according to the EU guidelines of current “Good Manufacturing Practice” (GMP). In 2008 the GMP unit at the Fraunhofer IGB was reconstructed, completely redesigned, extended from 150 to 215 m² and reaudited by the local authorities (Regierungspräsidium Tübingen). The areas for storage and quality control now cover 100 m², classified as class D (equivalent to US class 100,000), and are completely separated from the production unit. The production facilities of class C cleanrooms (equivalent to US class 10,000) and class B (equivalent to US class 1000) add up to 110 m². The new flexible designed areas allow an additional extension of the B area of 30 m² from the C area and v.v. The B area is divided into chambers with totally separated ventilation, therefore different manufacturing processes can be run simultaneously without the danger of cross-contamination. The unit is registered for work with genetically modified organisms up to biosafety level II (according to the German Gene Law).

Contract manufacturing or proprietary manufacturing

Since 2003 Fraunhofer IGB has been in possession of a Manufacturing Authorization according to §13 German Drug Law (AMG), for autologous chondrocyte transplants. We develop and validate manufacturing processes for our partners and – within the scope of this development, the subsequent clinical study and launching on the market – produce IMPs as a contract manufacturer in accordance with AMG or with the
German Medical Devices Act (MPG). Alternatively we can apply for a Manufacturing Authorization for your own products and operate as a manufacturing site at the Fraunhofer IGB. In this regard we have received three Manufacturing Authorizations in the past four years. Our customers are biotech and pharmaceutical companies as well as hospitals worldwide.

Quality assurance within all sectors

Extensive controls (bulk materials, intermediate and end products, in-process controls), complete documentation in accordance with the European guidelines, process validation and monitoring with qualified equipment and, last not but least, regular further training of personnel and self-inspections guarantee the quality and the safety of our products.

Projects

Melanocyte graft for therapy of vitiligo

Vitiligo is a chronic disorder involving the partial depigmentation of the skin, which has not been considered curable to date. A new therapeutic approach for the treatment of vitiligo is now available in the form of an autologous melanocyte graft developed at Fraunhofer IGB. The graft involves a melanocytes cell implant to reseed the diseased, pigment-free skin areas, promoting repigmentation of the skin and activating melanocyte growth. We are looking for cooperation with physicians/clinics interested in clinical efficacy studies.

Trachea patch for surgery

In collaboration with the surgical staff of the Robert Bosch Hospital Stuttgart, Department of General Thoracic Surgery of the Klinik Schillerhöhe, the Fraunhofer IGB develops a procedure for manufacturing an autologous implant for patients with severe tracheal injuries. Herefore, a biological vascularized cell-free scaffold is reseeded with the patient’s own cells. This trachea patch will be manufactured in the GMP unit for clinical studies funded by the German Federal Ministry of Education and Research (BMBF, Grant No. 031 55 75).

Collagen matrix as medical device

In cooperation with the company Amedrix we develop a collagen matrix for clinical use as a medical device.

References

Regeneration of bone with Tissue Repair Cells

Tissue Repair Cells are Aastrom’s bone marrow-derived autologous stem and progenitor cells. After ex vivo cultivation they are used for repairing bone fractures. The efficacy of these cells in the regeneration of vessels and in the heart area are being investigated in clinical trials. In contract for Aastrom, Fraunhofer IGB manufactures the cells for the trials in Europe.

Vascular grafts for bypass operations

Coating of PTFE vascular grafts with autologous endothelial cells to minimize the risk of thromboses is a proprietary technology of Vasotissue Technologies GmbH (VTT). In contract for Vasotissue we manufacture these grafts for application in cardiovascular disorders.

GMP  Good Manufacturing Practice
AMG  Arzneimittelgesetz (German Drug Law)
ATMPs Advanced Therapy Medicinal Products
IMPs  Investigational Medicinal Products
MPG  Medizinproduktegesetz (Medical Devices Act)
PTFE  Polytetrafluoroethylene
Services at a glance
- Process development of autologous transplants
- Manufacturing of cell- and matrix-based transplants
- Production and quality control of cell-based investigational medicinal products (IMPs) for phase I/II clinical studies
- Dealing with regulations/documentation
- Quality assurance

GMP at Fraunhofer IGB
- 215 m² flexible GMP unit
- Production facilities of class A in B cleanrooms
- Production facilities with class C cleanroom
- Separate units for quality control and storage (class D)
- Validated processes with qualified equipment
- Quality assurance system covering production, quality control and process development
- Laboratory tract of 500 m² for research and development

Quality assurance
- Qualified, trained personnel
- Facilities and equipment of defined quality status
- Documentation system based on specifications and standard operation procedures for manufacturing and packaging
- Production: in-process controls, prevention of cross-contamination
- Quality control of raw materials, packaging materials, intermediate, bulk and end products
- Certified suppliers
- Self-inspection

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