BIOTECHNOLOGY LABORATORIES OF THE SLOVAK ACADEMY OF SCIENCES

Šarišské Michaľany, Slovak Republic

BLOCK®
Clean Room Solutions


VYBUDOVANIE CENTRA VÝSKUMU
A VÝVOJA IMUNOLOGICKY
AKTÍVNYCH LÁTOK V
ŠARIŠSKÝCH MICHAĽANOCH
BLOCK
• Termín realizace •
7/2014 – 6/2015
• Investor •
Slovenská akadémia vied
• Generální zhotovitel •
BLOCK® a.s. – zriaďovateľ
organizačnej zložky, ako
vedúci účastník združenia
• Generální projektant •
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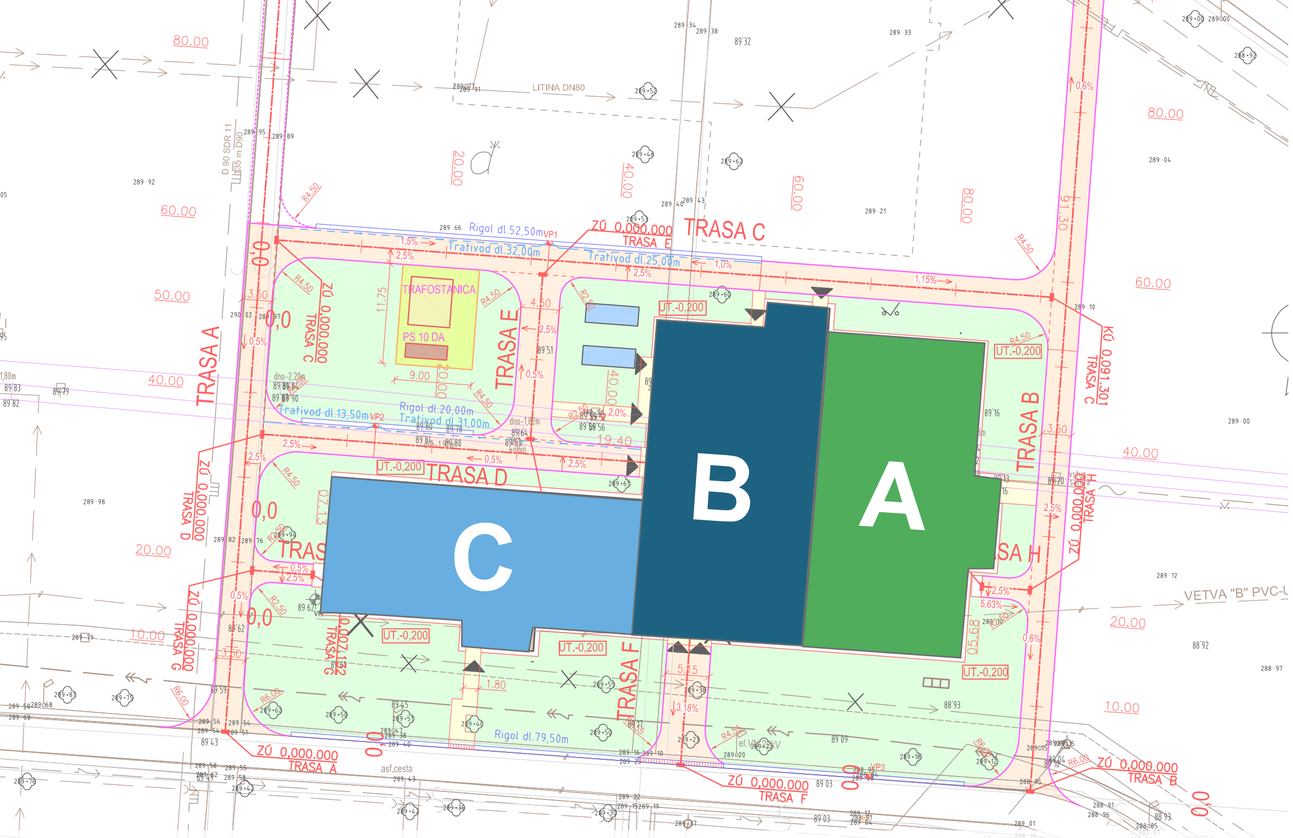
BIOTECHNOLOGICKÉ
LABORATÓRIA
SAV



The facilities of the SAS Biotechnology Laboratories are divided into Research (A), Development (B), and Analytical (C).

SAS BIOTECHNOLOGY LABORATORIES

UNIQUE HIGH-TECH LABORATORY FACILITIES FOR RESEARCH, DEVELOPMENT, AND BIOPHARMACEUTICAL CHARACTERISATION UNDER ASEPTIC CONDITIONS IN ACCORDANCE WITH LABORATORY AND GOOD MANUFACTURING PRACTICES.

BACKGROUND AND FOUNDATION OF BTL

Contemporary biomedical research both shapes innovation within the pharmaceutical industry as well as responding to its requirements.

New, safer, and more effective biopharmaceuticals are developed and prepared using modern biotechnological methods.

Based on the output of science and research, the pharmaceutical industry plays a significant role in the recovery and sustainability of economic growth in the European Union.

Slovakia is one of several EU countries that lag behind in their ability to effectively transfer the latest findings of biological and medical research into practice, which results in the pharmaceutical industry contributing significantly less than it could have been to the national economy.

OBJECTIVES AND SCOPE OF BTL

The Biotechnology Laboratories lead the way in research and development with the objectives and scope of increasing the quality of applied research in the development of biologically active substances with therapeutic effects or diagnostic uses, increasing the quality of technological processes and their preparation and analysis, and safeguarding effective transfer of acquired knowledge into practice.

Equipping of the Biotechnology Laboratories with modern infrastructure creates ideal conditions for the preparation, realisation, and implementation of domestic and foreign scientific research projects in the area of applied biological research. The professional and technical capabilities of the facilities provide the opportunity and environment for further education and professional growth of employees and students in the field of modern applied biological research.

The objectives and scope of the centre are also to expand scientific research cooperation between academic and commercial institutes both nationally and throughout the EU.

ORGANISATIONAL SUPPORT FOR BTL

The SAS Biotechnology Laboratories were built with financial support from the EU and the Slovak Republic as the outcome of the project “Centre for the research and development of immunologically active substances” (ITMS code 26220220188), co-financed by the European Regional Development Fund under measure OPVaV-2013 / 2.2.

Ministry of Education, Science, Research and Sport of the Slovak Republic

European Union
European Regional Development Fond

BTL SAS are part of the Department of Biotechnology Applications at the SAS Biomedical Research Centre, Institute of Virology, at its remote site in Šarišské Michaľany.

BTL SAS are open for cooperation with academic and industry partners in the field of applied biomedical research and development.

SAS

THE SLOVAK ACADEMY OF SCIENCES

The Slovak Academy of Sciences is an autonomous scientific institute focused on the development of science, education, culture, and economy. The primary aim of SAS and its organisations is to implement basic and applied research in a wide range of technical and natural sciences, humanities, and social sciences. Through its research, SAS seeks to develop knowledge at an international level while respecting the current needs of Slovak society and national culture. The organisations of the Academy cooperate with universities involved in education, especially the education of young scientists, as well as the pedagogical activity of universities. Through bilateral and multilateral domestic and international scientific projects, particularly those with EU funding, and through membership of international associations and institutes, SAS is developing extensive international cooperation and so places Slovak science in a transnational context.

PROJECT TIMELINE

01

REALISATION
OF THE RESEARCH CENTRE BUILDINGS TOOK PLACE OVER 12 MONTHS

PROJECT TIMELINE

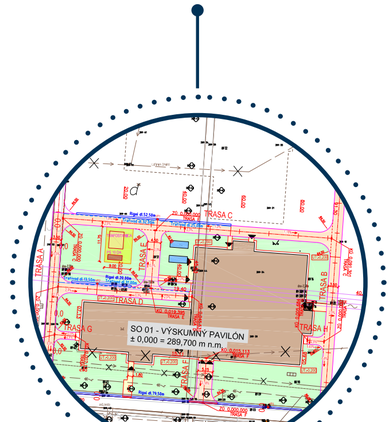
12/2013
- Notice of open competition for construction of the buildings according to the FIDIC Yellow Book (project and build).
- Investors provide a requirement specification for the three connected buildings, including situation, building design specification, and a list of technologies.

02/2014
- The BLOCK® proposal is submitted including layout design and schematics for pharmaceutical utilities and HVAC according to GMP guidelines.

03/2014
- Notice of the results of the selection process.

04/2014
- Work begins on the project for realisation of the construction.

06/2014
- First stage of the project for realisation of the construction is completed - groundworks project and reinforced concrete frame project.



07/2014
- The building site is received including valid permissi-on (arranged by the investor).
- On **14/07/2014 building work starts**
  - site preparation and laying of foundations.

08/2014
- Completion of bored piles foundation and work starts on erection of the reinforced concrete frame.

FOUNDATIONS

09/2014
- Second stage of the project for realisation of the construction is completed.
  - building envelope, utilities, and boiler room.
- Completion of reinforced concrete frame.
- Interior building works begin.

SUBSTRUCTURE

10/2014
- Completion of the project for realisation of the construction.
- Work starts on building cladding.

CLADDING

07/2014 | 08/2014 | 09/2014 | 10/2014 | 11/2014

BUILDING FRAME

ROOF

HVAC

11/2014
- Coordination of construction documentation with selected suppliers of technology directly purchased by the investor.
- Based on final documentation for building realisation, “documentation for the change of construction prior to finishing” was processed, based upon which the building authority issued approval.
- Installation of roof cladding and completion of building cladding.

MOVING OF CHILLERS
TRANSFORMER STATION

COOLING MACHINE ROOM

INTERIOR CONSTRUCTION, CLEAN ROOMS

12/2014 → 01/2015 → 02/2015 → 03/2015 → 04/2015

BOILER ROOM, REGULATION UNITS + COOLERS,
FITTING OF BUILDING AND TECHNOLOGY INSTALLATIONS

HVAC

12/2014
- Completion of roof cladding, closing of the building (windows and doors), and building heating is started.

HVAC

INSTALLATION OF TECHNOLOGY
AND COMPLETION OF INTERIOR
FITTINGS

04/2015

05/2015
- Building approval procedure initiated and approval granted with a certificate of occupancy.
- Validation procedure initiated.

05/2015

15.6/2015
- On **15/06/2015**, **the building is handed over** in time according to Contract for work, i.e. within 343 days of receipt of the building site.

09/2015
- Building enters operation, including validation protocols.

09/2015

REALISATION
OF THE RESEARCH CENTRE BUILDINGS TOOK PLACE OVER
12 MONTHS

FINAL BUILDING 02

BUILDING

Architectural design of the building

The architectural design respects and reflects that the research centre consists of three independent operational sections with their own separate entrances for employees and materials. Entrance to each section is achieved viaan externalenclosed staircase.

Separation of the centre into individual sections is reflected in the structural differentiation of each part, and also the use of two types of wall cladding: the three-floor sections arecompleted withverticalpanels while the two-floor sections completed with horizontal panels. The facade is finished in three colours: light grey, dark grey, and black. The alternating of coloured vertical and horizontal lines forms a colour structure across the facade. This structure disguises window and HVAC ventilation openings that are determined by the internal layout and positioning of technology, and that would otherwise make the exterior of the building look somewhat chaotic.

The building consists of two structural expansion units, while the layout is divided into three sections:

- **A (Research Laboratories)**, with three floors
- **B (Development Laboratories)**, with two floors
- **C (Analytical Laboratories)**, with three floors

BUILDING


BIOTECHNOLOGICKÉ
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Európska únia
Európsky fond regionálneho rozvoja
Podporujeme výskumné aktivity na Slovensku
Projekt je spolufinancovaný zo zdrojov Európskej únie
www.minedu.sk
MINISTERSTVO ŠKOLSTVA, VEDY, VÝSKUMU A ŠPORTU SLOVENSKEJ REPUBLIKY
Názov projektu:
Centrum výskumu a vývoja imunologicky aktívnych látok
Dátum začatia realizácie: 03/2014
Dátum ukončenia realizácie: 09/2015
Prijímateľ: Slovenská akadémia vied
Partner: Virologický ústav SAV
Miesto realizácie projektu: Šarišské Michaľany
ITMS: 26220220188
Výška spolufinancovania z EÚ: 21 246 356, 46 EUR
Predmet realizovaného projektu:
Hlavným cieľom realizácie projektu je vybudovanie Centra pre výskum a vývoj imunologicky aktívnych látok.
BIOTECHNOLOGICKÉ
LABORATÓRIA
SAV

A SECTION RESEARCH

The BTL Research Laboratories are divided into four separate units (A1, A2, A3, and A4) according to the work they are used for. There are clean rooms within each unit for work under aseptic conditions.This provides the circumstances for research and development activities that allow for Good Manufacturing Practise (GMP) certification of the laboratories.

The BTL Research Laboratories are focused on the research and development of:

- **biopharmaceuticals produced in eukaryotic systems (A1);**
- **new viral vaccines with emphasis placed on their effective preparation, and superior efficacy and safety (A4);**
- **therapeutic compounds of a bacteriological origin (A3);**
- **the final formulation of the above mentioned bioactive substances with a focus on their stability and increased efficacy (A2).**

A SECTION
FIRST FLOOR
RESEARCH

Section A – Research Laboratories – first floor part A1
Research into biopharmaceuticals in eukaryotic systems

This hygiene class “C” part of the research unitconsists of three processing areas. The section is used in the preparation of eukaryotic cells for subsequent use in infectious and non-infectious parts of the research and development “centre”. Open handling of cells (GMO2) is carried out using secure laminar boxes. The purpose of this section is the development of effective methods for production of immunologically active macromolecules, with the aim of optimising technological processes with a focus on the use of bioreactors. Optimisation of purification processes and development of biopharmaceutical formulations takes place during the final stage.

- ✓ Development and formulation of biopharmaceuticals in eukaryotic systems
- ✓ Growth factors
- ✓ Antibodies
- ✓ Immunomodulators

Section A – Research – first floor part A2
Filling of biopharmaceuticals and inactive vaccines, and media preparation

This part of the research unit includes a filling room with hygiene class “A/B”, and areas for washing, formulation, sterilisation, preparation of media, weighing, and related material and personnel entry rooms with hygiene class “C” or “B”. In future, there is the possibility of lyophilised production, necessitating the addressing of intended locations for the lyophilisation equipment and deep freezer.

- ✓ Formulation of biopharmaceuticals with improved stability and efficacy

A SECTION
FIRST FLOOR
RESEARCH

A SECTION
FIRST FLOOR
RESEARCH

A SECTION
FIRST FLOOR

RESEARCH

A SECTION
FIRST FLOOR
RESEARCH

A SECTION
SECOND FLOOR

RESEARCH

Section A – Research – second floor part A4
Research into eukaryotic vaccines

This operational unit for research into vaccines against viral infections is separated into infectious and non-infectious zones, with both having hygiene class “C”. The infectious zone consists of rooms for the preparation and primary propagation of viral vaccines and preparation of pilot virus batches, a darkened room for the scanning of eggs, and areas for antigen enrichment, clarification, concentration, and inactivation. The purification and formulation of vaccine antigens take place in the non-infectious zone where process methods will be developed and optimised. The infectious zone of the section for the production of eukaryotic vaccines must fulfil Biosafety level BSL2. There is an isolator for work categorised as Biosafety level BSL3 located in this area.

- ✓ Safer and more effective viral vaccines

Section A – Research – second floor part A3
Research into antimicrobial substances in prokaryotes

This operational unit for preparation and production of prokaryotic immunologically active substances consists of infectious and non-infectious zones, with both having hygiene class “C”. There is also a room for subcultures, which has hygiene class “B”. The infectious zone consists of areas for work with strains and cultivation of subcultures. The non-infectious zone includes a purification room and wash area. The infectious zone fulfils Biosafety level BSL2.

- ✓ Therapeutic and diagnostic compounds of a bacteriological origin

A SECTION
SECOND FLOOR
RESEARCH

A SECTION
SECOND FLOOR
RESEARCH

A SECTION
SECOND FLOOR
RESEARCH

A SECTION
SECOND FLOOR
RESEARCH

B SECTION DEVELOPMENT

The BTL Development Laboratories are dedicated to the upscaling of development activities in the field of preparation of new prophylactic compounds and are divided into an active part for work with active biological material, and aninactive part.

B SECTION
FIRST FLOOR
DEVELOPMENT

Section B – Development – First floor
Active part

The following processes are carried out in the active part:
- viral cultivation,receipt and inspection of incoming raw and intermediate materials;
- virus propagation using thermal chambers;
- inoculation of eggs and harvesting of allantoic fluid using a combined instrument;
- inoculum preparation;
- virus inactivation.

A steam autoclave is used in combination with the cleaning and sterilisation of containers for inactivation of produced waste.

Section B – Development – First floor
Inactive part

This unit is used for working with already inactivated viruses, with a specialisedpurification laboratory and an area for cleaning and sterilisation of centrifuge components and other laboratory devices.

There are further auxiliary technical rooms for PWA and water cooling machinery, WFI + PS and CIP/SIP machinery, and a central gas boiler.

B SECTION
FIRST FLOOR

DEVELOPMENT

B SECTION
FIRST FLOOR

DEVELOPMENT

B SECTION
FIRST FLOOR

DEVELOPMENT

C SECTION ANALYSIS

The Analytical Laboratories are divided into sections according to methodological focus and include a Documentation Department.

The BTL Analytical Laboratories provide:

- development and validation of new analytical methods for testing the efficacy of newly developed biologically active substances in vitro, and the qualitative and quantitative determination of their composition, the content of the active substance, and purity and sterility;
- implementation of new instruments and their validation and effective use in practice;
- analyses and control of outputs and activities conducted in the research and development laboratories:
  - physicochemical analysis,
  - microbiological analysis,
  - virologyanalysis,
  - molecular biological analysis;
- the processing, recording, and storage of all documentation related to BTL activity.

C SECTION FIRST FLOOR ANALYSIS

SECTION C – Analytical Laboratories – First floor

- Chemical analysis laboratories, i.e. laboratories for pH, TOC, and PLF control
- Classical methods laboratories – physical, and physicochemical methods
- Laboratory for the determination of bacterial endotoxins
- Laboratory for chemical analysis
- Physical methods laboratory – absorption spectroscopy and Hg determination
- Thin Layer Chromatography (TLC) laboratory – analytical chemistry, polarimetry methods, and High Performance Liquid Chromatography (HPLC)

C SECTION
FIRST FLOOR
ANALYSIS

C SECTION
FIRST FLOOR
ANALYSIS

C SECTION
SECOND FLOOR
ANALYSIS

Section C – Analytical Laboratories – Second floor

- Microbiological laboratories (growth, sterility, and serology testing)
- Virology laboratories
- Laboratory for clean cell substrate preparation
- Molecular biology laboratories (PCR analyses, analysis of nucleic acids and proteins)

C SECTION
SECOND FLOOR
ANALYSIS

TECHNICAL FACILITIES

Section A – Research – Third floor

- HVAC machine rooms

Section B – Development – First floor – Auxiliary technical areas

- PWA and water cooling machine room
- WFI + PS, and CIP/SIP machine room
- Central gas boiler room

Section B – Development – Second floor

- Central changing rooms for Section B
- HVAC machine rooms
- Boiler room
- CDA facilities

Section C – Analytical Laboratories – Third floor

- Cold storage+2 – +8 °C
- HVAC machine room

TECHNICAL FACILITIES

HVAC MACHINE ROOMS

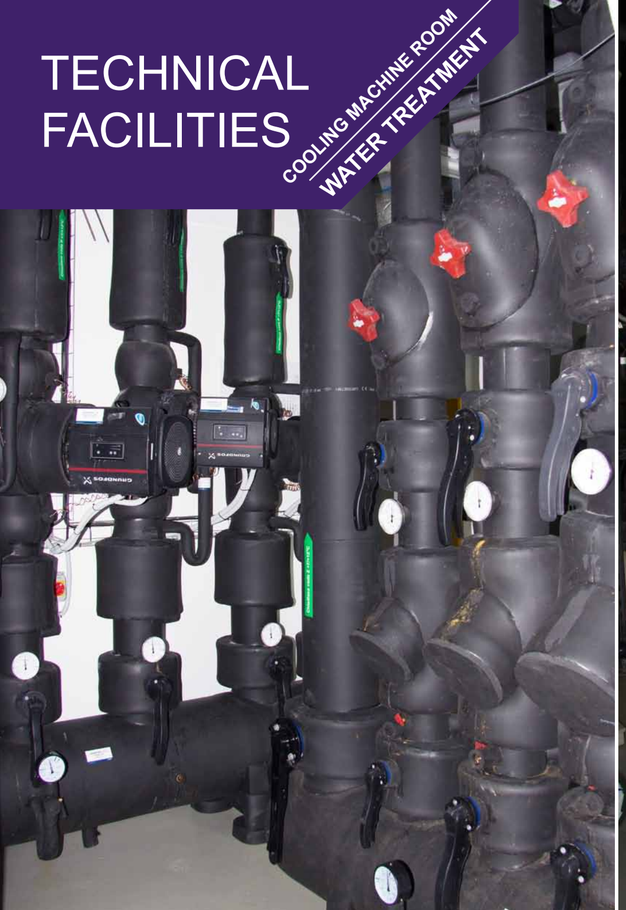
TECHNICAL FACILITIES

HVAC ON THE ROOF

TECHNICAL FACILITIES

COOLING MACHINE ROOM

WATER TREATMENT



TECHNICAL FACILITIES

BOILER ROOM

TECHNICAL FACILITIES

TRANSFORMER STATION

TECHNICAL FACILITIES

CHILLER

TECHNICAL FACILITIES

LIGHTNING RODS

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